Asymmetric Conjugate Addition of Arylboronates to α,β-unsaturated Enones Catalyzed by Substituted Binaphthols

by

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I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Conjugate addition reactions are one of the most widely used carbon-carbon bond forming reactions in organic synthesis. This reaction can form a chiral center and can be used for the synthesis of structurally complex compounds. Until now it has been necessary to use a chiral heavy metal catalyst in order to carry out asymmetric addition of aromatic groups to α,β-unsaturated enones via conjugate addition. Recently we have been successful in achieving the same task using an arylboronate as well as a catalytic amount of a chiral substituted binaphthol (BINOL). Using this reaction method great yields and enantioselectivities were achieved when diethyl phenylboronate was added to various enones and when various diethyl arylboronates were added to chalcone. This reaction is exciting because it eliminates the chance of having trace amounts of heavy metals in the final product, which is advantageous in such areas as the pharmaceutical industry.

Acknowledgements

I would like to thank Dr. Mike Chong giving me this thesis project and for his help and guidance throughout my time under his supervision. He was never too busy to talk about my chemistry even when he was swamped with work. For this I appreciate him and all that he has done very much. He has prepared me very well for my future as a chemist. I would also like to thank him for inviting me into his home several times for those great Chong lab Christmas parties and summer BBQ's. They were a blast!

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Last but not least, I would like to thank my close friends, my family, especially my parents, and my boyfriend Geoff, for all of their encouragement, love, and support. There is no way I will ever be able to repay them for everything they have done for me.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

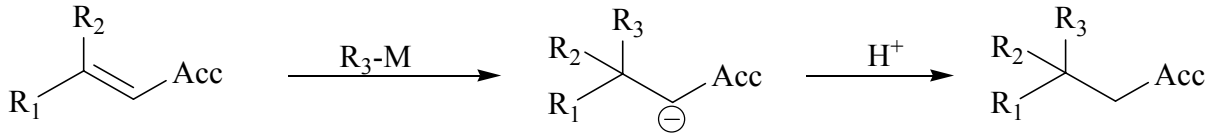
Å	angstrom
acac	acetylacetonyl
Ar	aromatic group
(aq)	aqueous
9-BBN	9-borabicyclo[3.3.1]nonane
Bn	benzyl
BINAL-H	binaphthol-modified aluminum hydride
BINOL	2,2'-dihydroxy-1,1'-binaphthol
Bu	butyl
n-BuLi	*n*-butyllithium
c	concentration
Calcd.	calculated
cm	centimetre
CuTC	copper thiophenecarboxylate
d	doublet
DFT	density functional theory
DMF	dimethylformamide
ee	enantiomeric excess
EI	Electron Ionization
eq	equivalent
er	enantiomeric ratio
Et	ethyl
et al.	et alii (and others)
eV	electron volts
FG	functional group

(g)	gas
g	gram
h	hour
HPLC	High Pressure Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
Hz	hertz
IPA	isopropyl alcohol
i-Pr	isopropyl
IR	Infrared Spectroscopy
J	coupling constant
L	ligand
m	multiplet
M^+	mass of compound
MCPBA	*meta*-chloroperbenzoic acid
MeOH	methanol
Me	methyl
MHz	megahertz
min	minute
mL	millilitre
mol	mole
MOM	methoxymethyl
m.p.	melting point
MS	molecular sieves
MS	Mass Spectrometry
NMR	Nuclear Magnetic Resonance
No.	number
Ph	phenyl

q	quartet
Rf	retention factor
s	singlet
t	triplet
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
v/v	volume/volume

1.0 Introduction

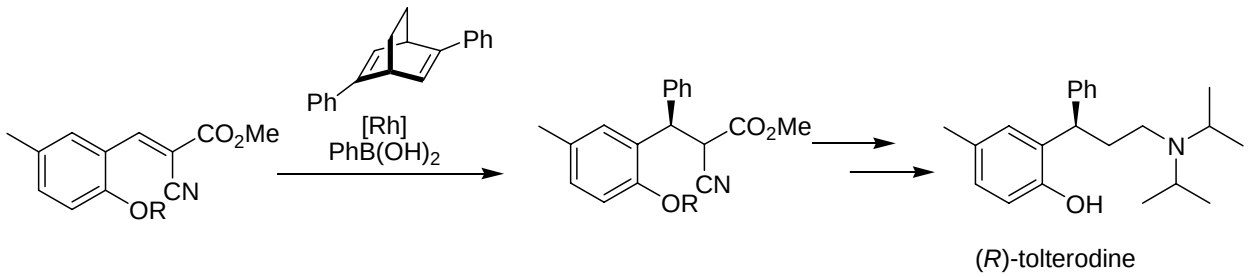
Conjugate addition (1,4-addition, Michael addition) reactions are one of the most widely used carbon-carbon bond forming reactions in organic synthesis (Figure 1.1).[1] This reaction is of great importance since most often a chiral center is created after the reaction has taken place,[2] and this reaction can lead to the synthesis of structurally complex compounds.[3] Much research has been carried out on the development of efficient enantioselective addition reactions since there are numerous donor and acceptor compounds that can be used for conjugate addition reactions.[2,3,4]



M = Metal	Acc = Acceptor
Li, Mg, Cu, Zn, Ru, etc.	COR, CO_2R, NO_2, etc.

Figure 1.1: Conjugate addition of a carbon nucleophile via an organometallic reagent to an olefin acceptor

Asymmetric conjugate addition reactions are key steps in the syntheses of various natural products, such as podophyllotoxin[5], and several pharmaceuticals, such as sertraline[6] and tolterodine.[7,8] An example of how this addition reaction is utilized in total synthesis can be seen in the reaction scheme for (*R*)-tolterodine (Scheme 1.1**)**.[8]

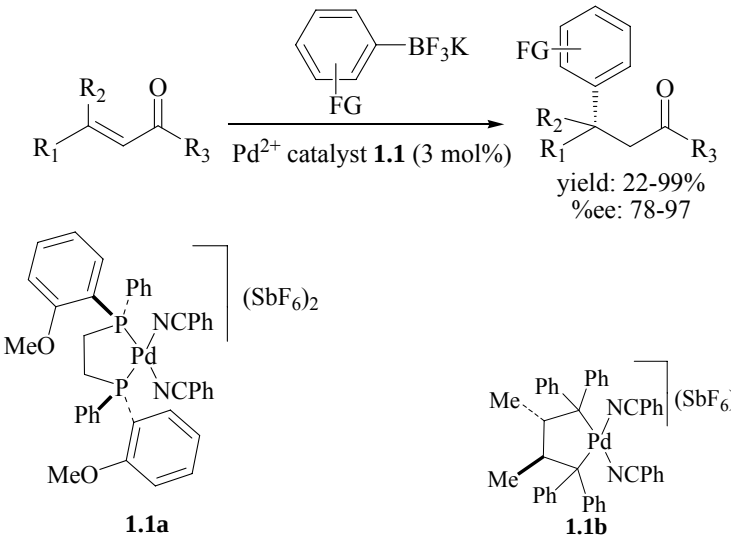


Scheme 1.1

1.1 Asymmetric Conjugate Addition Reactions

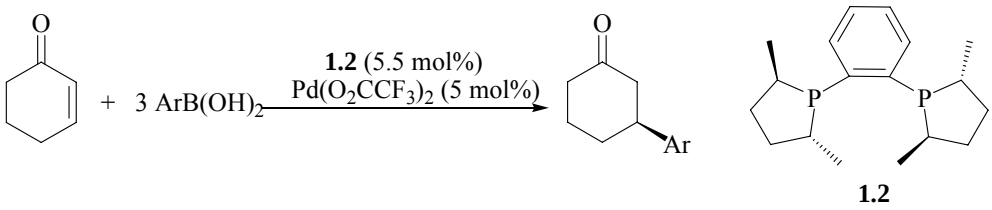
1.1.1 Palladium-Catalyzed Asymmetric Conjugate Addition

Palladium has been looked at as a catalyst for conjugate addition reactions since 1978 when palladium(II) acetate was used to add phenyl groups to α-substituted chalcone derivatives.[9] Only in the past few years have reactions been developed using palladium(II) complex catalysts that are enantioselective.[10,11] One such reaction was reported by Nishikata, Yamamoto and Miyaura, where potassium aryltrifluoroborates were added to enones using these palladium(II) complexes as catalysts (Scheme 1.2).[10] Overall this reaction gave decent to high yields and enantioselectivities.[10]



Scheme 1.2

This method was improved when arylboronic acids were used as the aryl source (Scheme 1.3).[11] This reaction, the first of its type, was reported by Gini, Hessen, and Minnaard.[11] The reaction gave yields greater than 99% and enantioselectivities up to 99%.[10] The advantage it has over the previously mentioned palladium-catalyzed reaction is that the arylboronic acids are more readily available than the aryltrifluoroborates.[11]



1.2

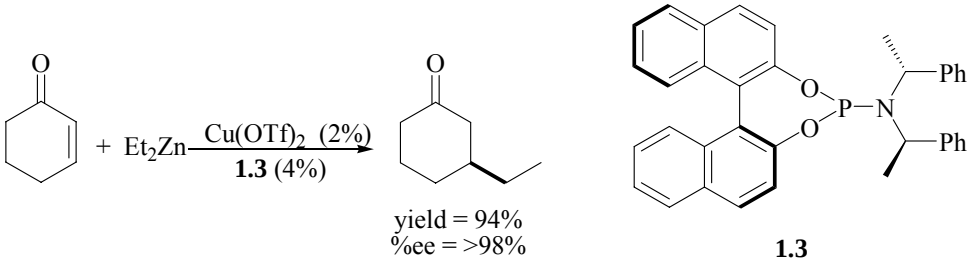
Ar	%yield	%ee
2-MeC_6H_4	>99	99 (*R*)
3-MeC_6H_4	>99	97 (+)
3-$MeOC_6H_4$	98	98 (+)

Scheme 1.3

1.1.2 Copper-Catalyzed Asymmetric Conjugate Addition

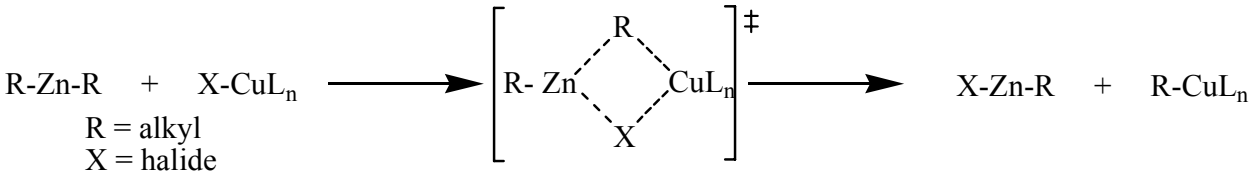
The pioneering asymmetric conjugate addition reactions using Grignard reagents to add various alkyl groups on to cyclic enones with the help of Cu catalysts were reported by Lippard *et al.* in 1988.[12] While the enantioselectivities of these conjugate addition reactions was very poor (1-14.5%), the reaction was influential in Cu-catalyzed conjugate addition research.[12] The next major breakthrough occurred in 1997 when Feringa *et al.* managed to carry out the first asymmetric conjugate addition reactions, using dialkylzinc reagents and Cu catalysts, that were

completely stereochemically controlled.[13] Enantioselectivities up to >98% were observed, and when this occurred the lesser isomer was undetectable (Scheme 1.4).[13]



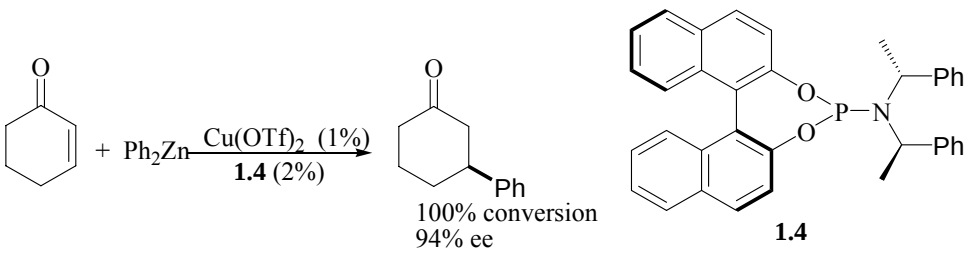
Scheme 1.4

The key step to conjugate addition reactions involving Cu catalysts is the transfer of the alkyl group from the alkyl-metal complex to the Cu catalyst to form the organocopper reagent.[4] The mechanism using a dialkylzinc reagent can be seen in Scheme 1.5.



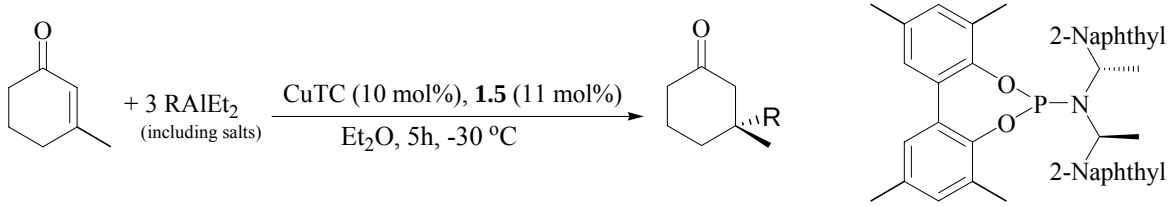
Scheme 1.5

While there has been a significant amount of research carried out on asymmetric conjugate addition reactions using Cu catalysts since Lippard's discovery, there are few examples of asymmetric arylation reactions using Cu catalysts and diarylzinc complexes.[14,15] The first reported copper-catalyzed arylation reaction, which was carried out by Reiser *et al.* in 2001, resulted in yields of only 53-73% and enantioselectivities of 59-74%.[14] A few years later Feringa was able to improve the efficiency of this reaction by modifying the conditions in which it was run.[15] He was able to obtain up to 100% conversion and enantioselectivities up to 94% (Scheme 1.6).[15]



Scheme 1.6

Alexakis *et al.* made an interesting discovery in 2008.[16] They were able to carry out copper-catalyzed asymmetric conjugate addition reactions where aryl groups were added via aryl aluminum reagents to trisubstituted cyclic enones.[16] This allowed them to construct cyclic ketones containing a quaternary center.[16] This asymmetric conjugate addition reaction involving arylaluminum reagents, chiral ligands and trisubstituted cyclic enones gave yields up to 87% and enantioselectivities up to 98.6% (Scheme 1.7).[16]



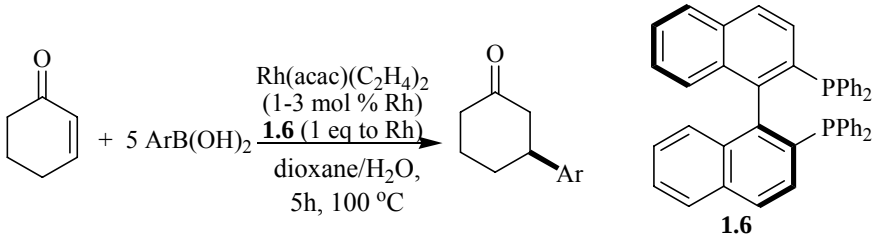
1.5

Entry	R	% yield	% ee
1	Ph	87	96.8
2	2-naphthyl	59	98.6

Scheme 1.7

1.1.3 Rhodium Catalyzed Asymmetric Conjugate Addition

Over the past ten years there have been many advancements in the Rh-catalyzed asymmetric conjugate addition of aryl reagents to *α,β*-unsaturated substrates. The initial reaction of this type was carried out by Hayashi *et al.* in 1998, using a Rh(I) catalyst that was formed in situ (Scheme 1.8).[17] This reaction was advantageous over previous reactions before this time because the organoboronic acids used were stable in the presence of oxygen and moisture, and they were much less reactive towards the enone in the absence of the chiral catalyst.[17] As well the Rh catalysts are able to add the aryl groups onto enones with high selectivity, which has been problematic with copper catalysts.[17] High yields and enantioselectivities were observed, even when various arylboronic acids were used.[17]

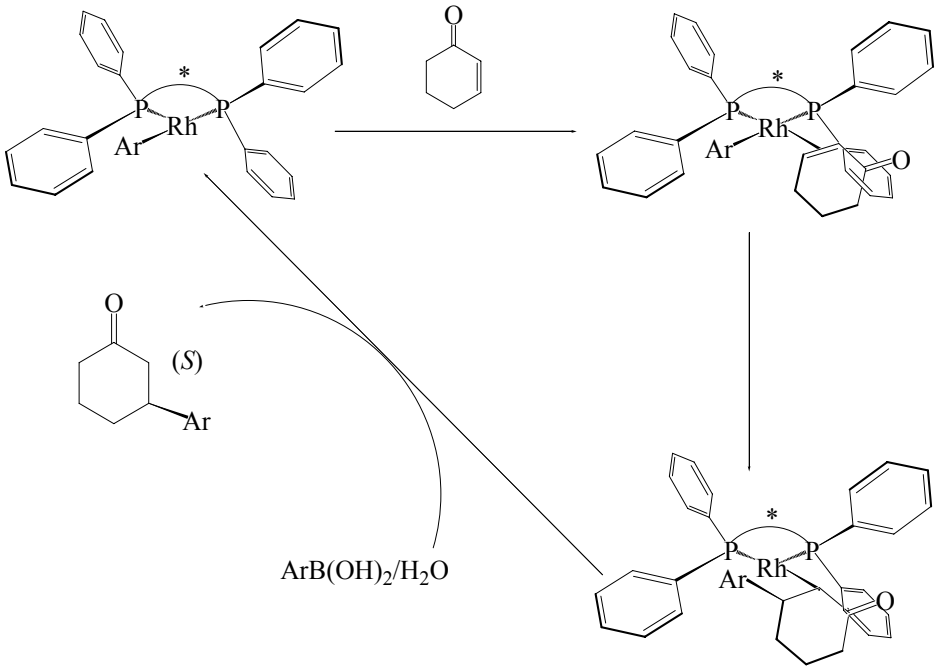


Ar	% yield	% ee
Ph	>99	97 (*S*)
4-MeC_6H_4	>99	97
3-$MeOC_6H_4$	97	96
3-ClC_6H_4	94	96

Scheme 1.8

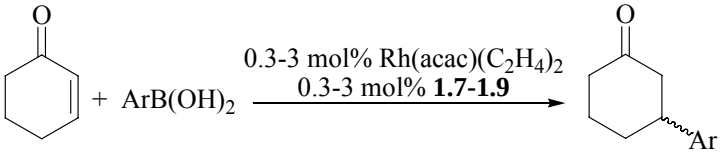
The catalytic cycle for this reaction (Scheme 1.9) involves the insertion of the enone carbon-carbon double bond into the aryl-rhodium complex, then migratory insertion of the aryl group, and then hydrolysis to release the newly formed aryl-substituted organic complex from

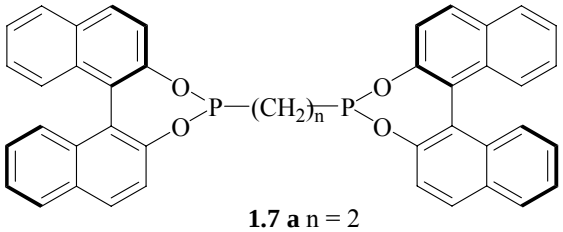
the rhodium complex.[17,18] The active aryl-rhodium complex is then regenerated by a transmetallation reaction with the arylboronic acid.[18]



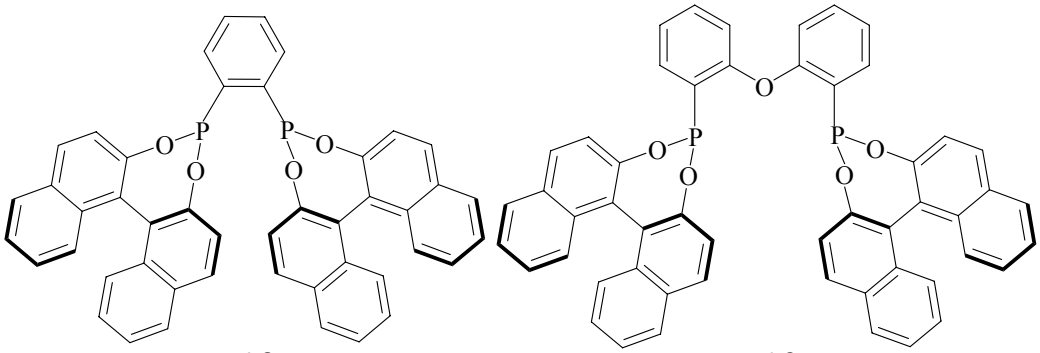
Scheme 1.9

Since the discovery of this asymmetric arylation reaction several chiral ligands have been tested and shown to be successful. Reetz, Moulin and Gosberg[19] found that when the achiral backbone was varied for the chiral BINOL-based diphosphonite ligands (ligands **1.7-1.9,** Scheme 1.10) used in Rh(I)-catalyzed arylboration reactions, good yields and high enantioselectivities were obtained, but the enantioselectivities were reversed. For example, when ligand **1.8** was used in this reaction the *S* enantiomer was produced, and when ligand **1.9** was used in this reaction under the same reaction conditions the *R* enantiomer was produced. The reaction conditions used were identical to the ones Hayashi *et al.* used when first discovering the asymmetric arylation reaction in 1998.[17,19] With the use of the BINOL-based diphosphonite ligands catalyst loadings as low as 0.3 mol% could be used without a loss in selectivity.[19]





1.7 a n = 2
b n = 4



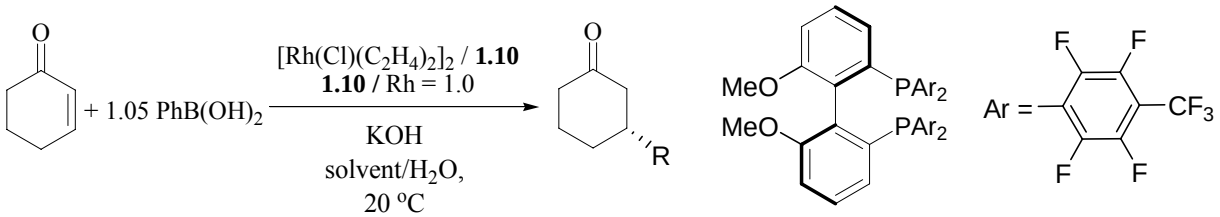
1.8 **1.9**

Ligand	Mol % of Ligand	% ee[a]
1.7a	3	95 (*S*)
1.7b	3	43 (*R*)
1.8	3	99 (*S*)
1.9	3	97 (*R*)
1.9	0.3	97 (*R*)

[a]100% conversion was achieved for each reaction represented in the table.

Scheme 1.10

In 2009 the Saki group developed an impressive Rh(I)-catalyzed reaction that used only 1.05 equivalents of phenylboronic acid, ran at room temperature, and added a phenyl group to a cyclic enone with good to excellent yields and excellent enantioselectivities (Scheme 1.11).[20] The chiral ligand used for this reaction was an electron-poor diphosphine ligand (**1.10**, Scheme 1.11).[20]



1.10

Entry	Rh (%)	KOH (%)	Solvent	Time (h)	% yield	% ee
1	3.0	30	dioxane	5	68	99
2	3.0	50	toluene	3	99	>99
3	0.2	20	toluene	1	98	>99
4	0.1	20	toluene	1	75	>99

Scheme 1.11

Rh(I)-catalyzed reactions have proved to be one of the most valuable asymmetric conjugate addition methods due to the fact that several types of catalysts and aryl-boronic compounds can be used. The enantioselectivities of these types of reactions have been high for several different types of ligands, the stereochemistry of the product can be tuned just by altering the ligand slightly, and the reaction temperature can be reduced to just room temperature when an electron-deficient diphosphine ligand is used.[17-20]

1.2 Previous Work on Allylboration, Alkenylboration and Alkynylboration on *α,β*-unsaturated Substrates

Over the past few years our group has developed several novel methodologies involving asymmetric conjugate addition reactions (Schemes 1.12-1.15).[21-26] They are the first reactions where BINOL and 3,3'-disubstituted BINOLs are used as the chiral catalysts to promote the addition of allylboronates, alkenylboronates, and alkynylboronates to *α,β*-unsaturated substrates instead of transition metal catalysts. [21-28]

The first reaction of this type that was a success was the enantioselective and regioselective addition of alkynylboronates to enones.[21] While the results using BINOL ranged from decent to great in terms of yield (38%-90%), they were disappointingly low in terms of enantiomeric selectivity (3-31% ee).[21] On the other hand, once substituents were added to the 3 and 3' positions on the BINOL ligand the enantioselectivities improved dramatically. The highest yields and enantioselectivities were seen when relatively electronegative aryl groups were placed at the 3 and 3' positions of the BINOL ligand.[21]

A cyclic 6-membered chair transition state similar to the ones proposed by Brown for the additions of alkynyl 9-BBN reagents to enones,[29] as well by Noyori for the asymmetric reduction of alkyl aryl ketones with BINAL-H,[30] is able to predict the stereochemistry that is observed for the alkynylation products. It is also able to rationalize the enhanced selectivity observed when BINOL has substituents located at the 3 and 3' positions (Figure 1.2).

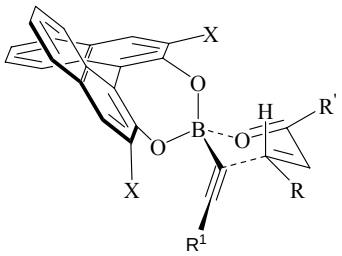
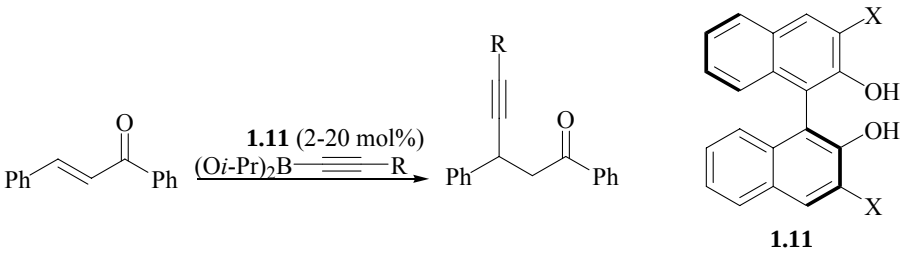


Figure 1.2: Cyclic 6-membered transition state.

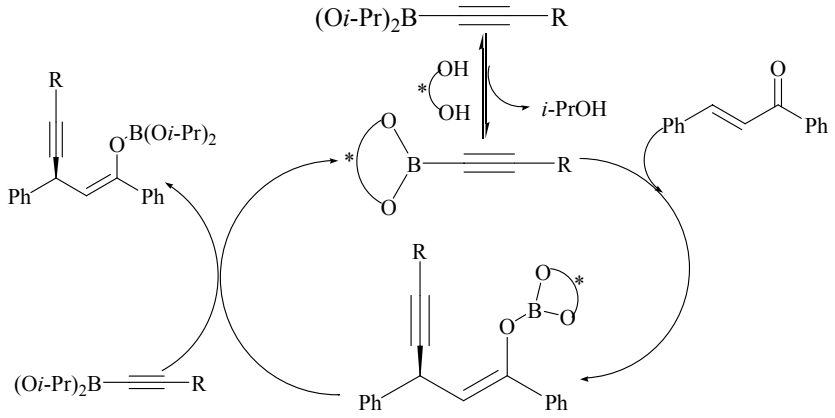
Recently it was discovered that this reaction proceeds efficiently when a catalytic amount of the BINOL and 3,3'-disubstituted BINOLs are used[23] instead of a stoichiometric amount as in the previously discussed reaction.[21] This catalytic method produces the desired product with good to great yields and excellent selectivities for various 3,3'-disubstituted BINOLs and enones (Scheme 1.12).[23] The proposed ligand-catalyzed cycle can be seen in Scheme 1.13.[23] This is a great achievement in asymmetric catalytic synthesis since this is the first example of organic ligand-accelerated catalysis using organoboronates.[23]



1.11

X (20 mol%)	R	% yield	% ee
Ph	C_6H_{13}	60	83
I	C_6H_{13}	95	87
I	Ph	95	82
I	CH_2OBn	91	95

Scheme 1.12



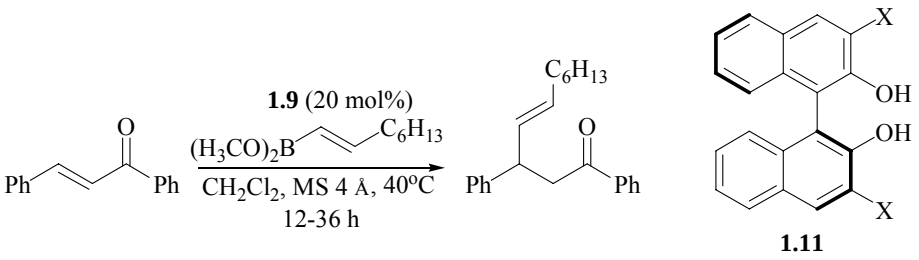
Scheme 1.13

Pellegrinet and Goodman carried out a computational analysis on the catalytic cycle proposed by the Chong group for the 3,3'-disubstituted BINOL-catalyzed asymmetric addition of alkynylboronates to enones which supported the Chong group's prediction.[31] The investigation of the limitations on the possible variations for the process and the direction of the stereoinduction involving the catalytic pathway was carried out by a study at the B3LYP/lacvp* level of theory and concluded that it was the pathway most favoured thermodynamically and kinetically.[31]

A similar method has been developed for the addition of allylboronates to carbonyl compounds using 3,3'-disubstituted BINOLs.[22,27] While it was the Chong group that developed the stoichiometric version of this reaction,[22] it was the Schaus group that reported the catalytic reaction involving the addition of allylboronates to ketones using 3,3'-disubstituted BINOLs.[27] For the stoichiometric allylboration reaction the results were very promising. Yields up to 98% were obtained and enantioselectivities up to >98% were recorded when the substituents at the 3 and 3' positions on the BINOL ligand were varied, along with the aldehyde and ketone substrates.[22] For the catalytic reaction that was reported by Schaus, yields up to 89% were reported and enantioselectivities up to 94% were observed.[27] The best results were observed when electronegative substituents were placed at the 3 and 3' positions.[27]

The Chong group was successful in further applying this method to the catalytic addition of alkenylboronates to enones via conjugate addition using a 3,3'-disubstituted BINOL (Scheme 1.14).[26] The asymmetric alkenylation of enones was carried out using BINOL, several different 3,3'-disubstituted BINOLs and various enones.[26] Overall this reaction had great yields and amazing enantioselectivities, especially when electronegative groups were placed on the BINOL

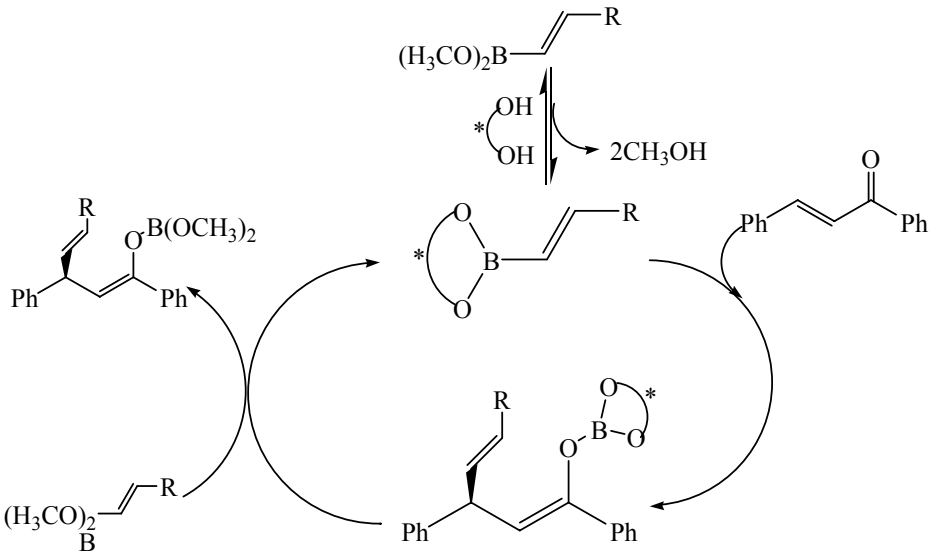
catalyst at the 3 and 3' positions. The catalytic cycle proposed for this reaction is similar to the one for the alkynylboration reaction (Scheme 1.15).[26]



1.11

X	% yield	% ee
H	<20	86
Ph	75	94
CF_3	>95	97
3,5-$(CF_3)_2C_6H_3$	>95	97

Scheme 1.14



Scheme 1.15

The alkenylboration reaction has been studied by Goodman and Pellegrinet as well.[32] They carried out a theoretical DFT study to gain a deeper understanding of what controls the

rates, selectivities and substituent effects in this reaction.[32] The calculations used in their study reproduced the experimental reactivity trends and enantiomeric ratios reported by Wu and Chong in 2007.[26,32] The study also revealed that the transition state structure is a sofalike transition structure instead of the chair transition structure that Wu and Chong predicted.[26,32]

Schaus *et al.* were able to take the alkenylboration and alkynylboration BINOL-catalyzed methods a step further and add alkenyl and alkynyl groups to acyl imines with good to great yields and great selectivities.[33] When the alkynyl groups were added to the acyl imines a BINOL-like catalyst (Figure 1.3) was used instead of the more common 3,3'-disubstituted BINOLs.[33] Schaus was also able to add aryl groups to acyl imines in the presence of a 3,3'-disubstituted BINOL catalyst, and these reactions resulted in great yields and selectivities.[33]

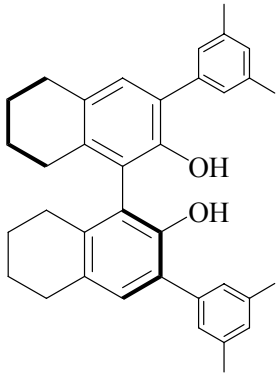


Figure 1.3 – BINOL-like catalyst used by Schaus *et al.* for alkynylboration of acyl imines.[33]

1.3 Thesis Topic

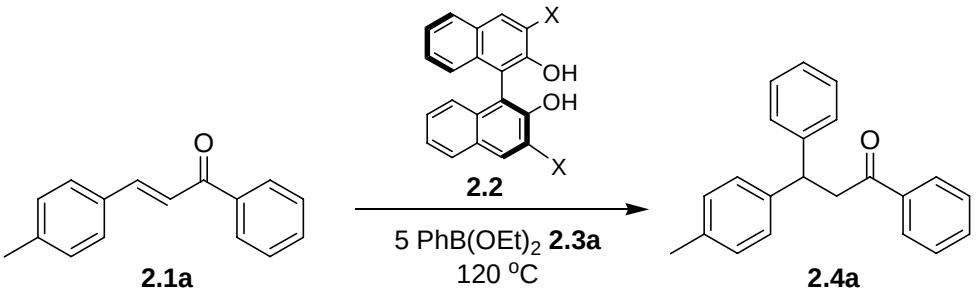
Since BINOL-catalyzed asymmetric conjugate additions using alkynylboronates[21,22] and alkenylboronates[26] have been successful for *α,β*-unsaturated enones and acyl imines,[33] and arylboration catalyzed by BINOLs has been successful for acyl imines,[33] it was proposed that the addition of aryl groups via arylboronates to *α,β*-unsaturated enones using a catalytic amount of BINOL would also be possible. This thesis project, which was to carry out the asymmetric conjugate addition of arylboronates to *α,β*-unsaturated enones using 3,3'-disubstituted BINOLs to catalyze the reaction, proved that it was possible. The reaction was first attempted with stoichiometric amounts of BINOLs and then the conditions were optimized so that the reaction proceeded with a catalytic amount of 3,3'-disubstituted BINOL to give good conversions and selectivities.

2.0 Results and Discussions

2.1 Initial Investigation into Arylboration

Initially, when determining whether the asymmetric conjugate addition of arylboronates to enones using catalytic amounts 3,3'-disubstituted BINOLs was possible, the reaction (Scheme 2.1) was carried out using enone **2.1a**, diethyl phenylboronate **2.3a**, and either 2 eq of BINOL or 1eq of 3,3'-disubstituted BINOLs. The 3,3'-disubstituted BINOLs used in the initial investigation were synthesized using methods carried out by Wu *et al*.[22]

The diethyl phenylboronate was synthesized using a method similar to one carried out by Wu and Chong.[26] Phenylboronic acid was refluxed with 1:2 EtOH:$CHCl_3$ (v:v) and 4Å sieves in a flame-dried flask under $Ar_{(g)}$ atmosphere for 48 hours. The reaction mixture was then filtered through a Schlenk filter and the excess solvent was removed by high vacuum. The diethyl phenylboronate produced was then stored under an $Ar_{(g)}$ atmosphere and used without further purification.



Scheme 2.1

The results from Table 2.1 show that this reaction was possible using an excess amount of BINOL and stoichiometric amounts of 3,3'-disubstituted BINOLs. The parent BINOL **2.2a** (Table 2.1, entry 1) gave good selectivity, but the conversion of starting material to product was not optimal. When looking at the results for BINOLs **2.2b** (Table 2.1, entry 2) and **2.2c** (Table 2.1, entry 3) they are similar in terms of their low conversions, but BINOL **2.2c** gives a higher enantioselectivity. BINOLs **2.2d** (Table 2.1, entry 4) and **2.2e** (Table 2.1, entry 5) give the two highest conversions out of the 5 BINOLs tested, but only BINOL **2.2d** gives a decent conversion with a product that has high enantioselectivity. The results obtained when BINOL **2.2e** is used show the highest conversion but the lowest selectivity. Overall, the best results were seen by BINOL **2.2d** since the reaction shows good conversion and good selectivity.

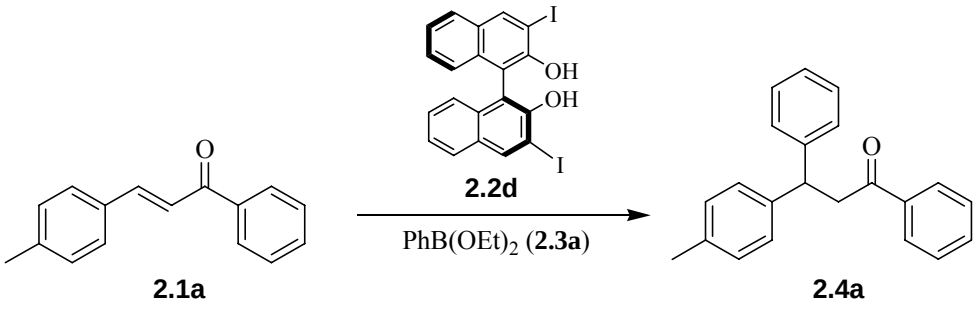
Table 2.1 – Reactions of BINOLs **2.2a-e** with **2.1a** and diethyl phenylboronate (**2.3a)**.

Entry	X (ligand)	BINOL Loading (mol %)	Time (h)	Conversion[a] (%)	Er[b]
1	H (**2.2a**)	200	96	< 50	9:91
2	CH_3 (**2.2b**)	100	72	34.5	12:88
3[c]	CF_3 (**2.2c**)	100	72	36	92:8
4	I (**2.2d**)	100	72	69	11:89
5	Ph (**2.2e**)	100	72	84	29:71

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on a Chiralcel OD column.
[c] *R*-BINOL was used.

2.2 Optimization of Reaction Conditions

The next step after establishing the most promising disubstituted BINOL was to optimize the reaction conditions. This was achieved by first exploring the effect of lowering the 3,3'-disubstituted BINOL loading, as well as varying the amount of boronate used, the temperature of the reaction, and attempting this reaction in the presence of a high-boiling solvent. The BINOL used for this set of tests was (*S*)-3,3'-diiodo-BINOL (**2.2d**) (Scheme 2.2) since it gave the best overall results (Table 2.1, entry 4).



Scheme 2.2

Table 2.2 – Reaction of BINOL **2.2d** with substrate **2.1a** and diethyl phenylboronate (**2.3a**) under various reaction conditions.

Entry	BINOL Loading (mol %)	Equivalents of 2.3a	Temp (^{o}C)	Time (h)	Conversion (%)[a]	Er[b]
1	200	5	110	24	100	8:92
2	100	5	110	72	69	11:89
3[c]	50	5	110	72	44	11:89
4	50	4	120	72	67	7:93
5	50	4	160	72	100	11:89

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on a Chiralcel OD column.
[c] 1,1,2,2-tetrachloroethane was used as the solvent.

A lot was learned from the results seen in Table 2.2. When comparing entries 1 and 2 in Table 2.2 it is seen that reducing the amount of BINOL **2.2d** from 200 mol% to 100 mol% when reacting enone **2.1a** with 5 equivalents boronate **2.3a** at a reaction temperature of 110 ^{o}C reduces

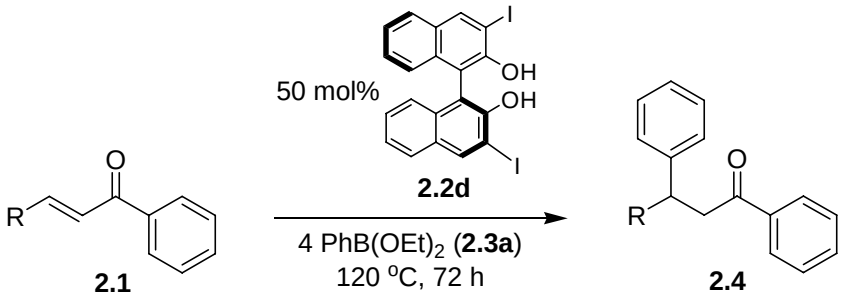
the conversion of substrate to product and reduces the selectivity of the reaction slightly. Entry 3 in Table 2.2 makes it clear that the combination of reducing the catalytic loading to 50 mol% and using high-boiling low-polarity 1,1,2,2-tetrachloroethane as a solvent does not optimize the conversion of product since these conditions give the lowest conversion. When the reaction was carried out without solvent at a temperature of 120 ^{o}C using enone **2.1a** and 50 mol% of BINOL **2.2d** (entry 4, Table 2.2), the reaction gave the best selectivity of 7:93. When the temperature of the reaction was increased from 120 ^{o}C to 160 ^{o}C (entry 5, Table 2.2), the conversion increased to 100%, but the reaction enantioselectivity decreased (when compared to the results in entry 4 of Table 2.2). Also, when the reaction temperature was increased from 120 ^{o}C to 160 ^{o}C (entry 5, Table 2.2), a side product was formed as well as the desired product in a 1:1 ratio. Therefore the overall optimal reaction conditions can be seen in entry 4 of Table 2.2.

2.3 Determination of a Background Reaction

In order to determine whether or not a background racemic reaction occurs during the arylboration reaction a control experiment was carried out using similar reaction conditions as seen in entry 4 of Table 2.2. The only difference in the reaction conditions was that no BINOL was used whatsoever. The results showed that after the reaction had run at 120 ^{o}C for 2 days the conversion of starting enone **2.1a** to ketone **2.4a** was 2.8% (as determined by ^{1}H NMR). Then the reaction temperature was increased to 165 ^{o}C and the reaction was run for four more days. After the four days it was determined by ^{1}H NMR that the reaction conversion had increased to 50%. Therefore it was determined that a background reaction did occur under the optimal reaction conditions (minus the presence of the BINOL catalyst), but it was very small so it should not affect the reaction method greatly.

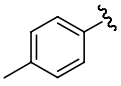
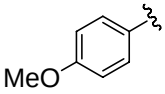
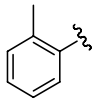
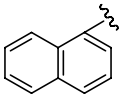
2.4 Substrate Structure and Ligand Effects

The reaction conditions used in Scheme 2.3 were considered the optimal conditions out of all that were tested (entries 1-5, Table 2.2) because they resulted in the most enantioselective reaction, a catalytic BINOL loading which is more favourable than a stoichiometric or excess loading, and a decent conversion of substrate to product after 72 hours.



Scheme 2.3

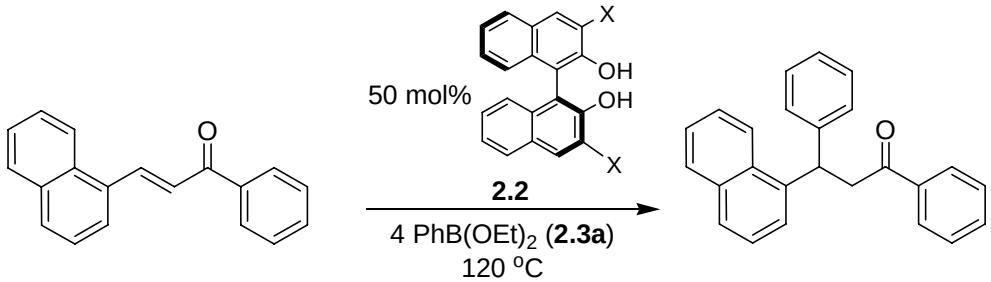
Table 2.3 – Reactions of enones **2.4a-d** with BINOL **2.2d** and diethyl phenylboronate **2.3a**.

Entry	R	Compound no.	Conversion[a] (%)	Yield (%)	Er[b]
1	 (**2.1a**)	**2.4a**	67	50	7:93
2	 (**2.1b**)	**2.4b**	85	52	10:90
3	 (**2.1c**)	**2.4c**	66	33	3:97
4	 (**2.1d**)	**2.4d**	83	19	6:94

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on a Chiralcel OD column.

When analyzing the results of the testing of different substrates using the same conditions, the best results on the whole occurred when diethyl phenylboronate is added to (*E*)-3-(1-naphthyl)-1-phenyl-prop-2-en-1-one (entry 4, Table 2.3). This is because when enone **2.1d** was used as the substrate the conversion was really good and the selectivity of the reaction was

great. The reactivity of enone **2.1b** (entry 2, Table 2.3) was greater than that of enone **2.1d**, but the selectivity was the lowest of all the reactions seen in Table 2.3. The enantioselectivity of the reaction involving enone **2.1c** was the highest out of all the reactions seen in Table 2.3, but the reactivity of the substrate was the poorest of all the enones tested. The yields of each reaction in Table 2.3 were low due to the inadequate isolation technique used at the time. When attempting to avoid loading the borizine that precipitated out from the reaction residue once it was dissolved in ether, some of the desired compound was not loaded onto the column which resulted in a lower overall yield. The isolation technique was improved by adding the borozine plus the ether-soluble material onto the column. The borozine did not affect the purity of the desired compound, and this improvement in the isolation technique gave better yields of the desired product. Besides the inadequate isolation technique used at the beginning of the project, the difficulty of separating the starting material from the product due to the fact that they have very similar Rf's also contributed to the lower isolated yields. The conversion and selectivity results seen in entry 4 of Table 2.3 prompted an investigation into how the conversions and selectivities changed when various 3,3'-disubstituted BINOLs were used to catalyze the reaction of enone **2.1d** with boronate **2.3a** at 120 ^{o}C (Scheme 2.4).



2.1d **2.4d**

Scheme 2.4

Table 2.4 – Reactions of enone **2.1d** with BINOLs **2.2d-h** and diethyl phenylboronate **2.3a**.

Entry	X (ligand)	Time (h)	Conversion[a] (%)	Yield (%)	Er[b]
1	I (**2.2d**)	72	83	19	6:94
2[c]	Br (**2.2e**)	32	100	45	99:1
3[d]	H (**2.2f**)	72	100	50	7:93
4	Cl (**2.2g**)	32	100	22	1:99
5	CN (**2.2h**)	5	100	53	3:97

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on a Chiralcel OD column.
[c] *R* BINOL was used.
[d] Ligand contains Br in the 6 and 6' positions.

BINOLs **2.2g** and **2.2h** were the only BINOLs used that had not been previously synthesized by Wu.[22-26] BINOL **2.2g** was synthesized using a method similar to the one used to synthesize BINOL **2.2d**.[22] BINOL **2.2d** was synthesized by Wu *et al.* in 2004.[22] The only major difference in the synthesis of BINOL **2.2g** compared to the synthesis of **2.2d** was that hexachloroethane was used instead of iodine.[22]

BINOL **2.2h** was synthesized using a new method. The synthesis followed a similar structure to those carried out by Wu *et al.*[22] where the MOM-protected disubstituted BINOL was first synthesized, then it was deprotected to give the desired disubstituted BINOL.

(*S*)-3,3'-Dicyano-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (**2.2i**) was synthesized by adding 3,3'-diiodo-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (1 eq), copper cyanide (4 eq) and DMF to a flame-dried flask under an $Ar_{(g)}$ atmosphere. The reaction mixture was heated to 80 ^oC and stirred overnight. The reaction was allowed to cool to room temperature, diluted with diethyl ether, then quenched with $NH_4Cl_{(aq)}$ at pH 8 then washed with $NH_4Cl_{(aq)}$ at pH 8, H_2O and brine. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (1/1 Et_2O/hexanes). This compound (**2.2i**) was then deprotected by placing it in a flask with a 1:1 (v/v) mixture of MeOH:THF and Amberlyst-15

(equal mass to **2.2i** placed in reaction), stirring the mixture at reflux overnight, then cooling the mixture to room temperature and filtering the mixture. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography to give BINOL **2.2h**.

The results from Table 2.4 showed that for the substrate used, the reaction gave overall great conversions and great selectivities, but not very great yields. The yields are still slightly low due to the same poor isolation techniques that were used when the reaction seen in Scheme 2.3 was carried out, and was remedied in an identical way later on in the project. 3,3'-Dibromo-BINOL (**2.2e**, entry 2, Table 2.4), 3,3'-dichloro-BINOL (**2.2g**, entry 4, Table 2.4) and 3,3'-dicyano-BINOL (**2.2h**, entry 5, Table 2.4) all gave higher conversions, lower reaction times and higher selectivities than 3,3'-diiodo-BINOL (**2.2d**), so they were looked at more closely. BINOL **2.2h** (entry 5, Table 2.4) was especially impressive since the reaction time was significantly shorter than the reactions using BINOLs **2.2d-2.2g** (entries 1-4, Table 2.4). The loading of BINOLs **2.2e,g,h** were decreased to 20 mol% to determine whether the reaction times and selectivities would differ from those seen in Table 2.4 (Table 2.5).

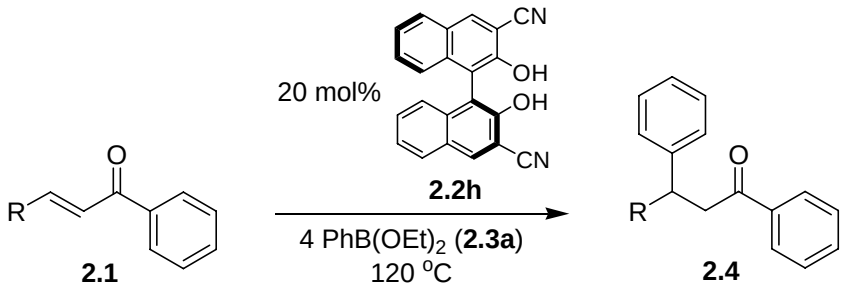
Table 2.5 – Reactions of enone **2.1d** with 20 mol% of BINOLs **2.2e,g,h** and diethyl phenylboronate **2.3a**.

Entry	X (ligand)	Time (h)	Conversion[a] (%)	Yield (%)	Er[b]
1[c]	Br (**2.2e**)	72	80	28	96:4
2	CN (**2.2h**)	5	100	50	3:97
3	Cl (**2.2g**)	32	100	86	2:98

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on a Chiralcel OD column.
[c] *R* BINOL was used.

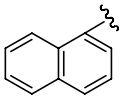
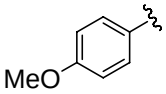
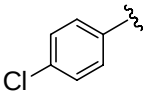
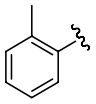
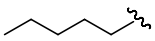
The results of these tests showed that the selectivities remained the same or decreased such a small amount that the advantage of the smaller catalyst loading outweighed the disadvantage of the lower selectivity. There was a major reaction time increase as well as a

conversion decrease when the loading of 3,3'-dibromo-BINOL (**2.2e,** entry 1, Table 2.5) was decreased, so it was ruled out as the optimal substituted BINOL to use for this reaction method. Both 3,3'-dichloro-BINOL (**2.2g,** entry 3, Table 2.5) and 3,3'-dicyano-BINOL (**2.2h**, entry 2, Table 2.5) gave practically the same selectivities when the loading was reduced from 50 mol% to 20 mol%. The high conversion, high enantioselectivity and very short reaction time for the reaction of enone **2.1d** with boronate **2.3a** at 120 ^{o}C in the presence of 20 mol% **2.2h** (entry 2, Table 2.5) prompted a study into how other enones would react under these new favourable conditions (Scheme 2.5).



Scheme 2.5

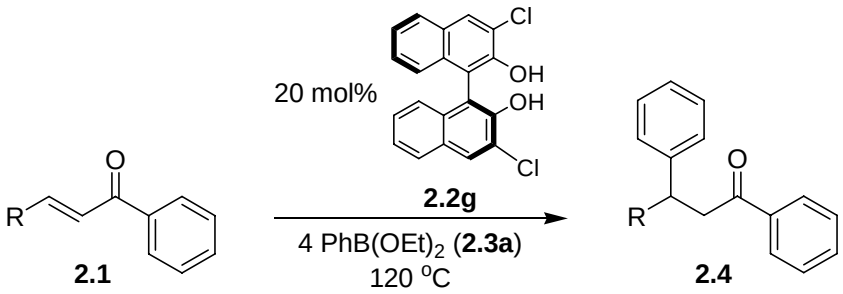
Table 2.6 – Reaction of enones **2.1b-h** with BINOL **2.2h** and boronate **2.3a** at 120 °C.

Entry	R	Compound no.	Time (h)	Conversion[a] (%)	Yield (%)	Er[b]
1	 (**2.1d**)	**2.4d**	5	100	90	3:97
2	 (**2.1b**)	**2.4b**	5	100	68	26:74
3	 (**2.1e**)	**2.4e**	5	100	75	21:79
4	 (**2.1c**)	**2.4c**	22	100	63	5:95
5	 (**2.1f**)	**2.4f**	5	100	85	15:85
6	 (**2.1g**)	**2.4g**	5	100	86	14:86
7	 (**2.1h**)	**2.4h**	5	100	61	14:86

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on a Chiralcel OD column.

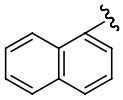
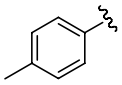
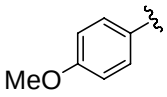
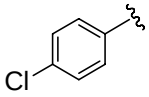
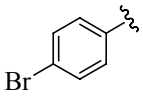
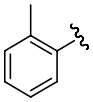
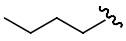
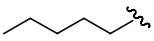
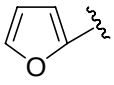
Unfortunately the results in Table 2.6 showed that while in general the reaction times were very short and the conversions were excellent, the selectivities were not promising. High selectivities were observed for more sterically demanding substrates (entries 1 and 4, Table 2.6) but for all the other enones tested the selectivities were much lower (entries 2,3,5-7, Table 2.6).

Since BINOL **2.2h** and BINOL **2.2g** gave similar results in terms of reaction enantioselectivity when reacted with **2.1d**, BINOL **2.2g** was reacted with the same enones as **2.2h** was in Table 2.6, as well as a few more, under the same reaction conditions seen in Scheme 2.5 (Scheme 2.6), in order to compare the results and determine which BINOL makes the best catalyst for the reaction of α,β-unsaturated enones with diethyl arylboronates.



Scheme 2.6

Table 2.7 – Reactions of enones **2.1a-j** with BINOL **2.2g** and diethyl phenylboronate **2.3a**.

Entry	R	Compound no.	Time (h)	Conversion[a] (%)	Yield (%)	Er[b]
1	 (**2.1d**)	**2.4d**	32	100	86	2:98
2	 (**2.1a**)	**2.4a**	72	100	90	9:91
3	 (**2.1b**)	**2.4b**	48	100	66	6:94
4	 (**2.1e**)	**2.4e**	48	100	74	10:90
5	 (**2.1i**)	**2.4i**	96	100	66	11:89
6	 (**2.1c**)	**2.4c**	48	100	75	1:99
7	 (**2.1f**)	**2.4f**	24	100	66	7:93
8	 (**2.1g**)	**2.4g**	72	83	72	12:88
9	 (**2.1j**)	**2.4j**	72	95	40	9:91
10	 (**2.1h**)	**2.4h**	24	100	54	9:91
11	 (**2.1k**)	**2.4k**	72	83	28	98:2

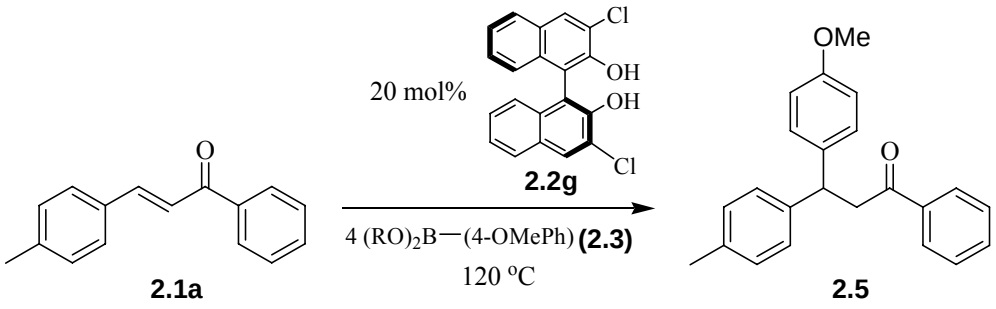
[a] Conversion was determined by ^{1}H NMR analysis.

[b] Er was determined by HPLC analysis on Chiralcel OD column.

As seen in Table 2.7, the reactions carried out with BINOL **2.2g** had longer reaction times than those carried out with BINOL **2.2h** (Table 2.6), but they had higher enantioselectivities. This showed that 3,3'-dichloro-BINOL **2.2g** was the best catalyst, out of all that were tested, to use for this reaction method. When looking at the results of Table 2.7 more closely, one would notice several trends. One is that the reactions with the highest enantioselectivities were the ones involving the more sterically demanding enones (entries 1 and 6, Table 2.7) or had a heteroaromatic group attached to the enone (entry 11, Table 2.7). The enone with the heteroaromatic group, which in this case was a furanyl group, gave a different elution result than the other ketone products resulting from the addition of **2.3a** to enone **2.1k**, it is assumed that the arylboration reaction carried out had the same facial selectivity (entry 11, Table 2.7). Enones with an electron donating group on the para position of an aromatic ring (entries 2 and 3, Table 2.7) give slightly higher selectivities than the enones with an electron withdrawing group on the para position of the aromatic ring (entries 4 and 5, Table 2.7). When looking at the results involving the enones containing an aliphatic group it can be seen that the enone with a methyl group attached gives the highest enantioselectivity when reacted with BINOL **2.2g** and boronate **2.3a** (entry 7, Table 2.7) while enones with the longer straight chain aliphatic groups had the same enantioselectivity when reacted under the same conditions (entries 9 and 10, Table 2.7), and the enone with the isopropyl group gave the lowest selectivity and reactivity (entry 8, Table 2.7). The low reactivity and selectivity of the enone with the isopropyl group (entry 8, Table 2.7) compared with the other enones tested in Table 2.7 could be due to the steric hindrance caused by the isopropyl group.

2.5 Effect of Aryl Group on Arylboration Reaction

Once it was established that the arylboration reaction worked very well for many enones, containing both aromatic and aliphatic groups (Table 2.7), the next action was to determine whether or not other aryl groups, besides a phenyl group, could be added to a α,β-unsaturated enones. During the first attempts to synthesize the various diethylboronates from commercial boronic acids using the same method that was used to synthesize diethyl phenylboronate, there were some complications. There was a lot of the arylboronic acid present at the end of the reaction, as well as monoesterified and diesterified product. Due to the initial complications, diethyl 4-methoxyphenylboronate as well as dibutyl 4-methoxyphenylboronate were synthesized in order to compare whether or not it was easier to make the dibutyl arylboronates and to compare the reactivity and selectivity of the reaction using diethyl 4-methoxyphenylboronate versus using dibutyl 4-methoxyphenylboronate. The dibutyl 4-methoxyphenylboronate turned out to be just as easy to synthesize as the diethyl 4-methoxyphenylboronate and both products showed no trace of the starting arylboronic acid. The only difference in the syntheses was for dibutyl 4-methoxyphenylboronate a 1:2 mixture of butanol:toluene was used instead of a 1:2 mixture of ethanol:chloroform. In order to compare the reactivities and selectivities of the two boronates they were reacted with enone **2.1a** in the presence of BINOL **2.2g** (Scheme 2.7).



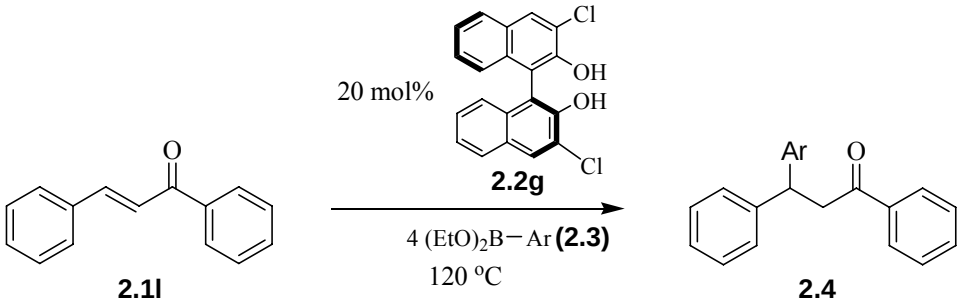
Scheme 2.7

Table 2.8 – Reaction of diethyl 4-methoxyphenylboronate (**2.3b**) vs reaction of dibutyl 4-methoxyphenylboronate (**2.3bb**).

Entry	R	Time (h)	Conversion[a] (%)	Yield (%)	Er[b]
1	Et	72	92	83	89:11
2	Bu	72	80	56	88:12

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on Chiralcel OD column.

The results in Table 2.8 show that the diethyl 4-methoxyphenylboronate (**2.3b**) has a higher reactivity than dibutyl 4-methoxyphenylboronate (**2.3bb**). After a Dean-Stark apparatus was added to the reaction set up for the synthesis of diethyl arylboronates, the syntheses of the other diethyl arylboronates (**2.3c-g**, Table 2.9) were successful. These diethyl arylboronates were then reacted with chalcone (Scheme 2.8) and the results are seen in Table 2.9.



Scheme 2.8

Table 2.9 – Reactions of enone **2.1l** with BINOL **2.2g** and diethyl arylboronates **2.3b-g.**

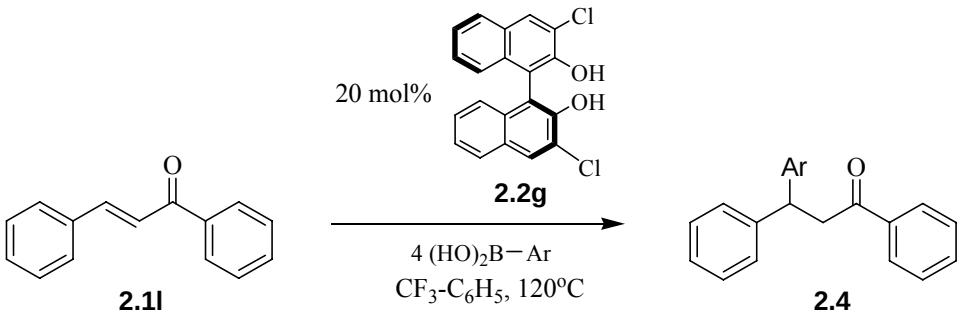
Entry	Ar	Compound no.	Time (h)	Conversion[a] (%)	Yield (%)	Er[b]
1	4-MeOPh (**2.3b)**	**2.4b**	29	100	88	89:11
2	4-MePh (**2.3c**)	**2.4a**	20.5	100	84	93:7
3	4-ClPh (**2.3d**)	**2.4e**	46	75	67	91:9
4	2-MePh (**2.3e**)	**2.4c**	48.5	100	70	95:5
5	3-MePh (**2.3f**)	**2.4l**	48.5	100	73	99.5:0.5
6	4-CF_3Ph (**2.3g**)	**2.4m**	73	25	21	91:9

[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on Chiralcel OD column.

The selectivities remained high when substituted aryl groups were added to chalcone, but not the reactivity (Table 2.9). When the arylboronate contains an electron withdrawing group in the para position (entries 3 and 6, Table 2.9) the reactivity was less than when electron donating groups are on the aromatic ring (entries 1,2,4 and 5, Table 2.9). Overall, Table 2.9 shows that this reaction works for a range of diethyl arylboronates when they are reacted with chalcone in the presence of BINOL **2.2g** at a temperature of 120 ^{o}C.

2.6 Reactivity of Arylboronic Acids in Arylboration Reaction

The conditions were changed slightly to explore how the addition of a variety of commercially available arylboronic acids to chalcone (Scheme 2.9) compared to the addition of the diethyl arylboronates when it came to yields and selectivities. A high-boiling solvent was needed to create a reaction medium for the solid reactants.



Scheme 2.9

Table 2.10 – Reaction of enone **2.1l** with commercially available arylboronic acids and BINOL **2.2g.**

Entry	Ar	Compound no.	Time (h)	Conversion[a] (%)	Yield (%)	Er[b]
1	4-MeOPh	**2.4b**	87	65	50	83:17
2	4-MePh	**2.4a**	87	100	28	86:14
3	4-ClPh	**2.4e**	87	45	38	88:12

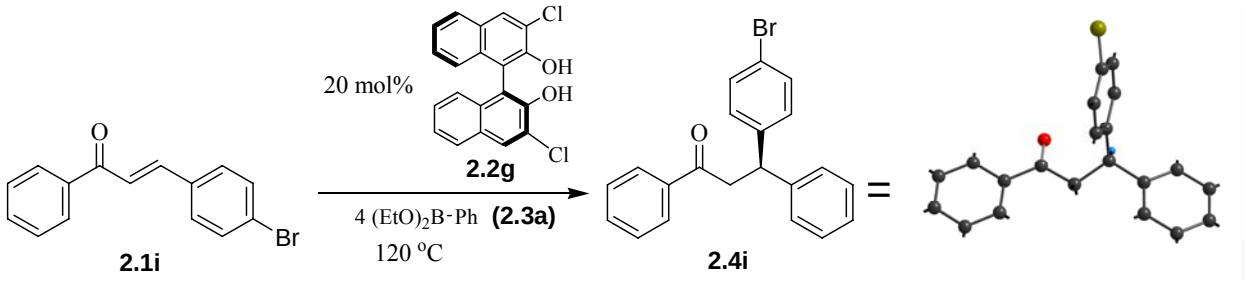
[a] Conversion was determined by ^{1}H NMR analysis.
[b] Er was determined by HPLC analysis on Chiralcel OD column.

While using the arylboronic acid would be easier since the boronic acids are commercially available while the arylboronates have to be synthesized from the corresponding arylboronic acids, the reactions proceeded with lower conversions, yields and selectivities. This is clear when comparing the results from Table 2.9 and Table 2.10. The use of diethyl arylboronates gave better selectivities and eliminated the need for the use of toxic solvents.

2.7 Determination of Absolute Configuration

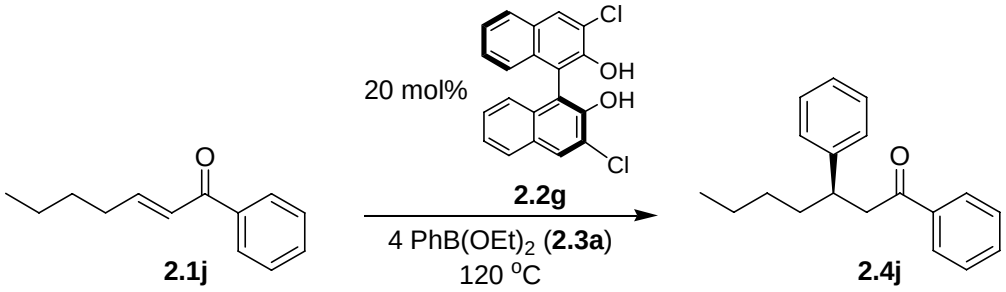
When comparing the results from Tables 2.7 and 2.9 it can be seen that when the phenyl ring is added to a variety of substrates via diethyl phenylboronate in the presence of (*S*)-BINOL (Table 2.7) most often the major enantiomer elutes from the HPLC column second, while when a variety of substituted aryl rings are added to chalcone via diethyl arylboronates in the presence of (*S*)-BINOL (Table 2.9) the major enantiomer elutes first from the HPLC column. As well, when

4-chlorophenyl)-1,3-diphenylpropan-1-one (**2.4e**) was synthesized by reacting diethyl phenylboronate (**2.3a**) with (*E*)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (**2.1e**) in the presence of (*S*)-3,3'-dichloroBINOL (entry 4, Table 2.7) the major enantiomer elutes from the HPLC column second, and when the same addition product **2.4e** was synthesized by reacting chalcone with diethyl 4-chlorophenylboronate (**2.3d**) in the presence of BINOL **2.2g** the major enantiomer eluded first from the HPLC column (entry 3, Table 2.9). From these two results it could be assumed that the major enantiomer formed in entry 4 of Table 2.7 was the opposite of the major enantiomer formed in entry 3 of Table 2.9. In order to determine which enantiomer is the major one formed when a phenyl group via diethyl phenylboronate is added to several different substrates in the presence of (*S*)-BINOL 3-(4-bromophenyl)-1,3-diphenylpropan-1-one (Table 2.7, entry 5) was recrystallized two times in order to give the pure major enantiomer (the purity was determined by HPLC analysis on a Chiralcel OD column). Then the absolute configuration was determined by X-ray crystallography. From the results it was concluded that the major enantiomer formed when the diethyl phenylboronate was reacted with (*E*)-3-(4-bromophenyl)-1-phenylprop-2-en-1-one, the major product was (*R*)-3-(4-bromophenyl)-1,3-diphenylpropan-1-one (Scheme 2.10).



Scheme 2.10

The absolute configuration of the product of this arylboration reaction is further supported by the results observed for the reaction of (***E***)-1-phenylhept-2-en-1-one (**2.1j**) with diethyl phenylboronate (**2.3a**) in the presence of (*S*)-3,3'-dichloroBINOL (entry 9, Table 2.7). When the product is run through the Chiralcel OD HPLC column the major enantiomer elutes second, and when Waldmann *et al.* synthesized the same product they observed that the major enantiomer eluted first from their Chiralcel OD HPLC column and they found that the major enantiomer for the reaction was the (*S*)-enantiomer.[34] From their results it could be concluded that the major enantiomer formed when enone **2.1j** is reacted with arylboronate **2.3a** in the presence of (*S*)-BINOL **2.2g** is the (*R*)-enantiomer (Scheme 2.11).[34]



Scheme 2.11

2.8 Proposals for Mechanistic Details

The proposed catalytic cycle for this reaction is similar to that proposed for alkynylboration[23] and alkenylboration[26], since these are all similar reactions (Figure 2.1).

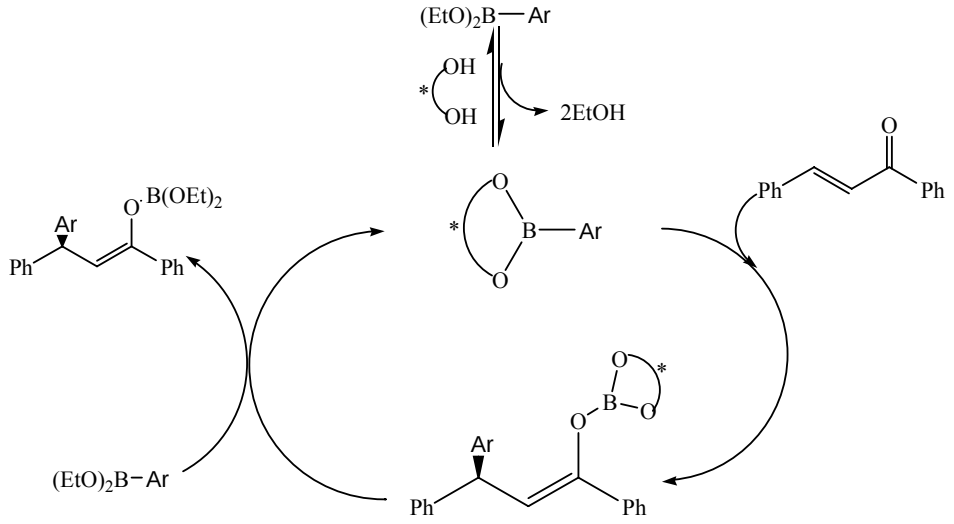


Figure 2.1: Proposed catalytic cycle for arylboration.

The proposed transition state for this reaction method (Figure 2.2) is also similar to the one proposed for alkynylboration[23] and akenylboration[26].

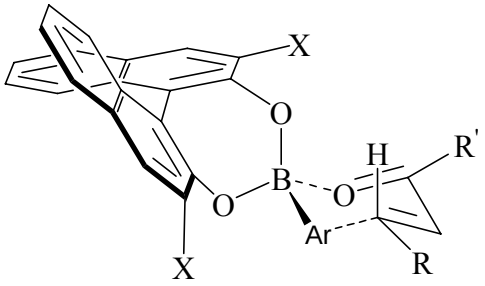


Figure 2.2: Proposed transition state for arylboration.

The X-ray crystallography results support the proposed transition state, since when using (*S*)-3,3'-Dichloro-BINOL to catalyze the addition of a phenyl group via diethyl phenylboronate to the substituted chalcone (enone **2.1i**) the major enantiomer produced was the *R* enantiomer,

and when the substituted aryl groups were added to chalcone using the same (*S*)-BINOL catalyst, the *S* enantiomer was the major product.

2.9 Future work

2.9.1 Further Optimization of Arylboration Reaction

One aspect of the arylboration reaction that could be improved upon is the reactivity of the substituted BINOL. 3,3'-Dicyano-BINOL (**2.2h**) was tested first with various enones because it had such a short reaction time with enone **2.1d** as well as great enantioselectivity (entry 2, Table 2.5). Unfortunately the results showed that the great enantioselectivities were only observed with sterically hindered enones (entries 1 and 4, Table 2.6) and those enones that were less sterically hindered did not give as high selectivities (entries 2,3,5-7, Table 2.6). 3,3'-Dichloro-BINOL (**2.2g**) was then tested with various enones because when it was reacted with enone **2.1d** it also had great selectivity but with a longer reaction time (entry 2, Table 2.5). When BINOL **2.2g** was tested with the same enones as BINOL **2.2h**, as well as a few more, it was observed that all the reaction had very good selectivities (Table 2.7) but the reaction times were much longer than those seen when BINOL **2.2h** was used to catalyze the reaction. If there was a way to combine the selectivity of BINOL **2.2g** with the reactivity of BINOL **2.2h** the optimal BINOL could be produced. This could possibly be achieved by placing the cyano ligands on the 6,6' positions on the BINOL and placing the chloro ligands on the 3 and 3' positions on the BINOL (Figure 2.3). This would allow for the electron withdrawing capability of the cyano ligand to be combined with the small size of the chloro ligands, which allows for less steric hindrance when it is reacted with the boronate and enone.

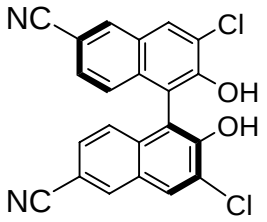
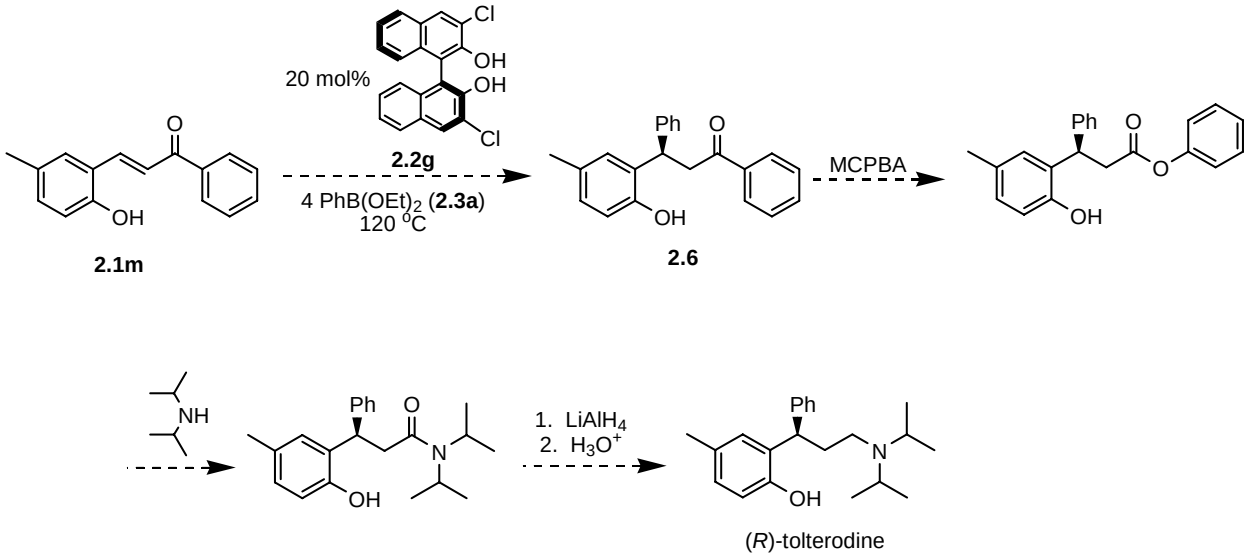


Figure 2.3 – Possible BINOL to test in arylboration reaction.

2.9.2 Practical Applications of Arylboration Reaction

2.9.2.1 Synthesis of (*R*)-tolterodine

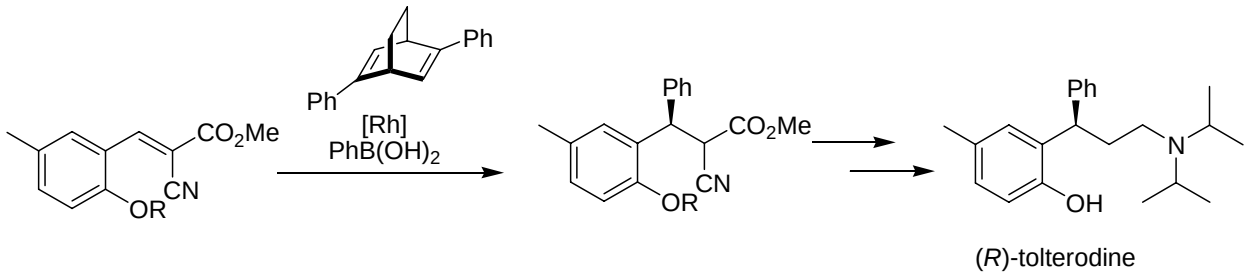
Since the arylboration reaction has been optimized to a point where various diethyl arylboronates could be added to chalcone with good yields and selectivities, and diethyl phenylboronate could be added to various enones with good yields and selectivities, it is time to try improving on some natural product syntheses using this reaction. One such case would be with the synthesis of (*R*)- tolterodine (Scheme 2.12).



Scheme 2.12

Using the arylboration reaction compound **2.6** could be synthesized by reacting enone **2.1m** with diethyl phenylboronate (**2.3a**) in the presence of the BINOL **2.2g** catalyst. Then **2.6**

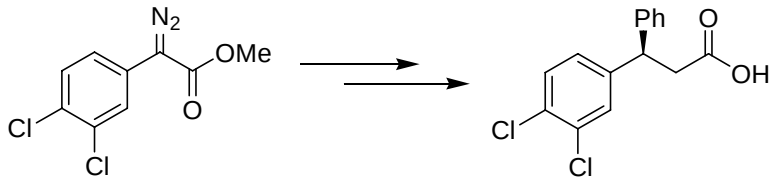
could undergo a Baeyer Villiger oxidation reaction and be reacted with a secondary amine to form the amide form of (*R*)-tolterodine. After that if the amide was then reacted with $LiAlH_4$ it should form (*R*)-tolterodine. This an improvement upon Hayashi's synthetic pathway (Scheme 2.13) because it uses no heavy metals, which is a great advantage since (*R*)-tolterodine is a pharmaceutical compound.[35]



Scheme 2.13

2.9.2.2 Synthesis of Indatraline

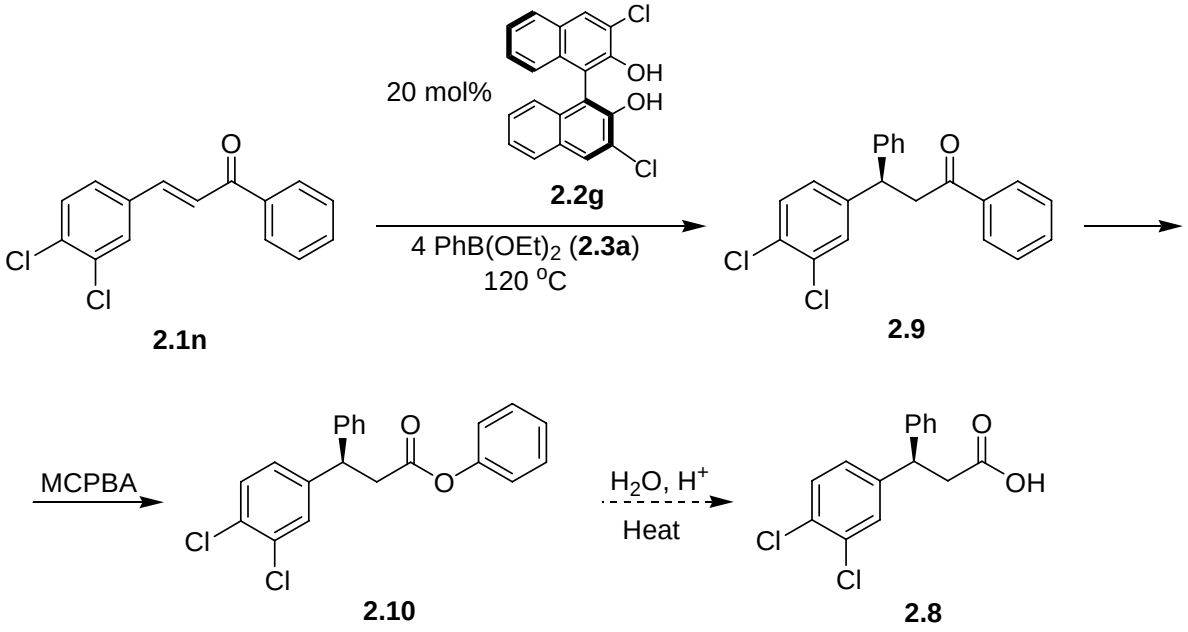
The synthesis of Indatraline could also be improved by using the arylboration method. One intermediate compound that Davies[36] uses to synthesize Indatraline is very similar to the ketones produced when arylboration is carried out on α,β-unsaturated enones. In Davies' synthetic pathway it takes five steps to go from compound **2.7** to compound to compound **2.8** (Scheme 2.14).[36]



2.7 **2.8**

Scheme 2.14

If enone **2.1n** was used instead, compound **2.8** could be synthesized in three steps (Scheme 2.15).



Scheme 2.15

Bobby Guobadia, a former member of the Chong group, successfully synthesized ketone **2.9** from enone **2.1n** using the arylboration reaction method and got great results.[37] The yield was 0.61g (86%) and the er for this reaction was 91:9.[37] After this he carried out a Baeyer Villiger reaction on ketone **2.9** to produce ester **2.10**.[37] This reaction showed a 51% conversion (conversion was determined by ^{1}H NMR) from **2.9** to **2.10**.[37] While the conversion is lower than one would desire, the reaction could possibly be optimized in order to obtain a more favourable yield. This was the last step Guobadia carried out in the synthetic pathway proposed for Indatraline. After **2.10** is synthesized it could be heated up with H_2O and acid to produce **2.8**. There are only three more steps that need to be carried out in order to synthesize the desired pharmecutical Indatraline from **2.8**.[36]

2.10 Conclusion

This thesis project was a success. Several aryl groups were added to chalcone **2.1k** using the corresponding diethyl arylboronates (**2.3b-g**) and BINOL **2.2g** with good yields and selectivities. As well, diethyl phenylboronate was added to enones **2.1a-j** using a catalytic amount of BINOL **2.2g** resulting in great yields and selectivities. Further work could be carried out though on optimizing the arylboration reaction using α,β-unsaturated enones. The substituted BINOL could be improved upon so the reactions have great selectivities and shorter reaction times. As well, this new reaction method could be used in the total synthesis of pharmaceuticals, as well as natural products, in order to improve on synthetic pathways already developed.

3.0 Experimental

General Experimental

All reactions were performed using flame-dried glassware under an argon atmosphere. Chiral 3,3′-disubstituted binaphthols were synthesized using procedures carried out by Wu *et al.* unless otherwise noted.[21] ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 MHz and 75 MHz, respectively, unless otherwise specified. Mass spectra were recorded on a Kratos MA890 mass spectrometer using electron impact (EI, 70 eV) ionization unless otherwise specified. Optical rotations were recorded in cells with 10 cm path length on an Autopol III automatic polarimeter. The commercially boronic acids used for the diethyl arylboronate syntheses were bought from Matrix Scientific.

General Procedure for Diethyl arylboronate synthesis:

Air sensitive arylboronates were prepared by refluxing the corresponding arylboronic acid with 1:2 (v:v) of EtOH (10mL/g):$CHCl_3$ (20mL/g) and 4Å sieves in a flame-dried flask under argon atmosphere for 48 hours. This reaction is based on one carried out by Wu *et al.*,[25] but instead of distilling the boronate after 48 hours, the excess solvent was removed under high vacuum and the boronate left in the flask was used without further purification and stored under $Ar_{(g)}$.

Large Scale Synthesis for Diethyl Phenylboronate:

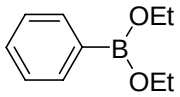
Phenylboronic acid (11.65 g , 0.1 mol, 1 eq) was refluxed in 126 mL (2.2 mol, 22 eq) of EtOH and 252 mL of $CHCl_3$, and in the presence of 72 g of 4Å sieves in a flame-dried flask under argon atmosphere. After 48 hours the reaction was filtered through a Schlenk filter and the

excess solvent was removed by placing the filtrate under high vacuum to provide 16 g of a light brown oil (80% yield).

Small Scale Synthesis of Diethyl 3-methylphenylboronate

3-Methylphenylboronic acid (2.0 g , 0.015 mol, 1 eq) was refluxed in 20mL (0.55 mol, 37 eq) of EtOH and 40 mL (0.50 mol, 33 eq) of $CHCl_3$, and in the presence of 4Å sieves in a flame-dried flask under argon atmosphere. After 48 hours the reaction was filtered through a Schlenk filter and the excess solvent was removed by placing the filtrate under high vacuum to provide 1.83 g of a yellow oil (65% yield).

Diethyl phenylboronate (2.3a)

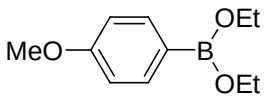


^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (s, 2H), 7.41 (s, 3H), 4.13 (q, J = 6.8 Hz, 4H), 1.32 (t, J = 6.6 Hz, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 133.2, 129.4, 127.7, 60.2, 17.5

^{11}B NMR (96 MHz, $CDCl_3$): δ 28.6

Diethyl 4-methoxyphenylboronate (2.3b)



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 4.11 (q, J = 7.0 Hz, 4H), 3.81 (s, 3H), 1.29 (t, J = 6 Hz, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 160.7, 135.2, 60, 54.9, 17.5

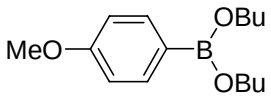
^{11}B NMR (96 MHz, $CDCl_3$): δ 28.3

Monoesterified product:

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H), 1.33 (t, J = 6 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 162, 136.2, 59.1, 17.1

Dibutyl 4-methoxyphenylboronate (2.3bb)



^{1}H NMR (300MHz, $CDCl_3$): δ 7.61 (d, J = 8.7 Hz, 2H), 6.90 (d, J = 6.8 Hz, 2H), 4.02 (t, J = 6 Hz, 4H), 3.81(s, 3H), 1.62 (m, 4H), 1.43 (m, 4H), 0.946 (t, J = 4.5 Hz, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 160.7, 135.3, 113.1, 64.1, 54.9, 33.9, 19, 13.8

^{11}B NMR (96 MHz, $CDCl_3$): δ 28.2

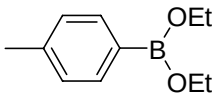
Monoesterified product:

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 3.99 (t, J = 6 Hz, 4H), 3.79 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 161.9, 136.2, 113.2, 63.1, 33.6, 18.9

^{11}B NMR (96 MHz, $CDCl_3$): δ 18.2

Diethyl 4-methylphenylboronate (2.3c)



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62 (d, J = 7.8 Hz, 2H), 7.26 (d, J = 7.8 Hz, 2H), 4.17 (q, J = 7.1 Hz, 4H), 2.44 (s, 3H), 1.36 (t, J = 7.1 Hz, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 139.3, 133.4, 128.6, 60.1, 21.4, 17.5

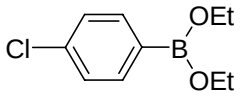
^{11}B NMR (96 MHz, $CDCl_3$): δ 28.6

Monoesterified product:

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 8.1), 4.16 (q, J = 7 Hz, 2H), 2.42 (s, 3H), 1.40 (t, J = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 141.1, 134.6, 128.7, 59.2, 21.5, 17.2

Diethyl 4-chlorophenylboronate (2.3d)



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 4.06 (q, J = 7 Hz, 4H), 1.26 (t, J = 7 Hz, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 135.6, 134.6, 127.8, 60.2, 17.4

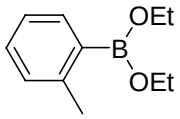
^{11}B NMR (96 MHz, $CDCl_3$): δ 28.1

Monoesterified product:

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 7.5, 2H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 135.7, 128.0,

Diethyl 2-methylphenylboronate (2.3e)



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25 (m, 4H), 3.96 (q, J = 7.5 Hz, 4H), 2.41 (s, 3H), 1.29 (t, J = 6.6 Hz, 3H)

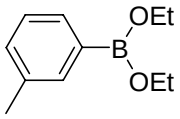
^{13}C NMR (75 MHz, $CDCl_3$): δ 139.7, 130.9, 129.1, 128.5, 124.8, 60.2, 21.9, 17.4

^{11}B NMR (96 MHz, $CDCl_3$): δ 29.9

Monoesterified product:

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.09 (q, J = 6 Hz, 2H), 2.51 (s, 3H), 1.34 (t, J = 7.5 Hz, 3H)

Diethyl 3-methylphenylboronate (2.3f)



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (m, 2H), 7.23 (m, 2H), 4.17 (q, J = 6 Hz, 4H), 2.45 (s, 3H), 1.36 (t, J = 7 Hz, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 136.9, 133.8, 130.15, 130.07, 127.7, 59.9, 21.4, 17.5

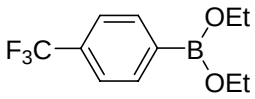
^{11}B NMR (96 MHz, $CDCl_3$): δ 28.6

Monoesterified product:

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.42 (s, 3H), 1.42 (t, J = 6 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 137.0, 135.2, 131.8, 131.5, 127.9, 59.3, 21.3, 17.1

Diethyl 4-trifluoromethylphenylboronate (2.3g)



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, J = 7.9 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 4.08 (q, J = 7 Hz, 4H), 1.28 (t, J = 7.1 Hz, 6H)

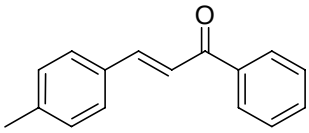
^{13}C NMR (75 MHz, $CDCl_3$): δ 134.6, 122.3, 59.6, 17.2

^{11}B NMR (96 MHz, $CDCl_3$): δ 28.2

General Procedure for Synthesis of Enones:

Aldehyde (1 eq), ethanol (0.013 mL/mmol), 50% NaOH (0.010 mL/mmol) and 1.05 eq acetophenone were added to a reaction flask. Reactants were stirred at room temperature until reaction was complete, then the solid obtained was filtered and recrystallized from hexanes.

(*E*)-1-phenyl-3-*p*-tolylprop-2-en-1-one (2.1a)



m.p. 90-92 ^{o}C

IR (KBr): 1656, 1512, 984, 694

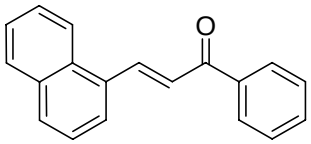
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, J = 7.1 Hz, 2H), 7.78 (d, J = 15.7 Hz, 1H), 7.56-7.45 (m, 6H), 7.21 (d, 8.0 Hz, 2H), 2.38 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 190.6, 144.9, 141.0, 138.3, 132.6, 132.1, 129.7, 128.5, 128.4, 121.1, 21.5

MS *m/z* (relative intensity): 222 (M^+, 66), 207 (M^+-CH_3, 100), 145 (M^+-Ph, 29), 105 ($PhCO^+$, 13), 77 (Ph^+, 18)

HRMS *m/z* calcd. for $C_{16}H_{14}O$ (M^+): 222.1045. Found: 222.1051.

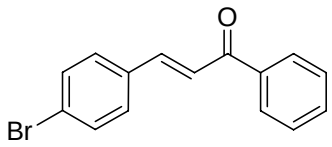
(*E*)-3-(naphthalen-1-yl)-1-phenylprop-2-en-1-one (2.1d)[22]



^{1}H NMR (300 MHz, $CDCl_3$): δ 8.66 (d, J = 15.4, 1H), 8.25 (d, J = 8.2 Hz, 1H), 8.07 (d, J = 8.0 Hz, 2H), 7.93-7.87 (m, 3H), 7.65-7.49 (7H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 190.3, 141.7, 138.1, 133.7, 132.8, 132.3, 131.7, 130.8, 128.7, 128.6, 128.5, 126.9, 126.3, 125.4, 125.1, 124.6, 123.5

(*E*)-3-(4-bromophenyl)-1-phenylprop-2-en-1-one (2.1i)



m.p. 119-121 ^{o}C

IR (KBr): 1659, 664 cm^{-1}

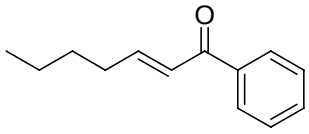
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, J = 7.9 Hz, 2H), 7.73 (d, J = 15.7 Hz, 1H), 7.61-7.48 (m, 7H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 190.1, 143.3, 137.9, 133.7, 132.9, 132.2, 129.7, 128.6, 128.4, 124.7, 122.5

MS *m/z* (relative intensity): 286 (M^+, 100), 285 (M^+-H, 45), 207 (M^+-Br, 65), 179.1 (24), 178.1 (19), 105 ($PhCO^+$, 35), 102 (30), 77 (Ph^+, 26)

HRMS *m/z* calcd. for $C_{15}H_{11}{}^{79}BrO$ (M^+): 285.9995. Found: 285.9991

Synthesis of (*E*)-1-phenylhept-2-en-1-one (2.1j)



IR (neat): 2871, 1621, 1004

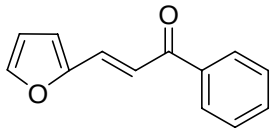
^1H NMR (300 MHz, $CDCl_3$): δ 7.91 (d, J = 7.0 Hz, 2H), 7.53 (t, J = 6.7 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 7.10-7.00 (m, 1H), 6.85 (d, J = 15.3 Hz, 1H), 2.30 (q, J = 6.8 Hz, 2H), 1.52-1.33 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 190.8, 150.0, 138.0, 132.5, 128.4, 125.8, 32.5, 30.2, 22.2, 13.8

MS *m/z* (relative intensity): 188 (M^+, 76), 159 (M^+-C_2H_5, 41), 145 (M^+-C_3H_7, 24), 131 (M^+-C_4H_9, 15), 105 ($PhCO^+$, 100), 83.91 (23), 77 (Ph^+, 33)

HRMS *m/z* calcd. for $C_{13}H_{16}O$: 188.1202. Found: 188.1203

Synthesis of (*E*)-3-(fran-2-yl)-1-phenylprop-2-en-1-one (2.1k)[38]



2-Furaldehyde (1.53 mL, 18.4 mmol), acetophenone (2.15 mL, 18.4 mmol), NaOH (0.98 g, 1.84 mmol), MeOH (20 mL) and H_2O (20 mL) were stirred in a round-bottomed flask at room temperature overnight. The reaction was quenched with 6 M HCl (~0.3 mL), then the product was extracted with dichloromethane (3 x 50 mL). The organic layers were combined, dried over

$Na_2SO_{4(s)}$, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (1:10-1:7 Et_2O:hexane) to provide 3.2 g of (*S*)-3-(furan-2-yl)-1,3-diphenylpropan-1-one as a colourless oil (89% yield)..

^1H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, J = 8.50 Hz, 2H), 7.61-7.41 (m, 6H), 6.695 (d, J = 3Hz, 1H), 6.50-6.48 (m, 1H).

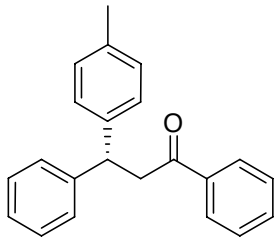
^{13}C NMR (75 MHz, $CDCl_3$): δ 189.8, 151.6, 144.9, 138.1, 132.7, 130.6, 128.6, 128.4, 119.2, 116.2, 112.6.

General Procedure B

α,β-Unsaturated enone (0.387 mmol, 1 eq), 3,3'-disubstituted BINOL (0.0744 mmol, 20 mol%) and diethyl arylboronate (1.548 mmol, 4 eq) were added to the reaction flask and heated up to 120°C. Crude material was purified by flash column chromatography on silica gel (hexane/Et_2O) to give the addition product.

The enantiomeric purities of the products were determined by HPLC analysis (4.6 x 250 mm ChiralCel OD, hexane/*i*-PrOH = 99.6/0.4 ~ 98.8/1.2 v/v).

(*R*)-1,3-diphenyl-3-*p*-tolylpropan-1-one (2.4a)



This compound (a pale yellow solid) was prepared in 90% yield from (*E*)-1-phenyl-3-*p*-tolylprop-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-

binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ -28.0 (9:91 er, c 2.9, $CHCl_3$)

m.p. 76-78 ^oC

IR (KBr): 1688, 1598, 700 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J = 7.8 Hz, 2H), 7.55 (t, J = 7.0 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.28 (d, 4.1 Hz, 4H), 7.21-7.17 (m, 3H), 7.09 (d, J = 4.0 Hz, 2H), 4.82 (t, J = 7.3 Hz, 1H), 3.74 (d, J = 7.3 Hz, 2H), 2.30 (s, 3H)

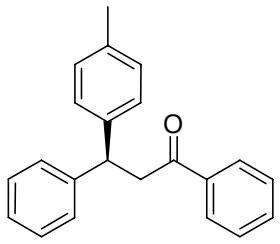
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.0, 144.4, 141.1, 137.1, 135.8, 133.0, 129.2, 128.6, 128.5, 128.0, 127.8, 127.7, 126.3, 45.5, 44.8, 21.0

MS *m/z* (relative intensity): 300 (M^+, 85), 194 (23), 181 (M^+-$PhCOCH_2$, 100), 165 (21), 105 ($PhCO^+$, 46), 77 (Ph^+, 13)

HRMS *m/z* calcd. for $C_{22}H_{20}O$ (M^+): 300.1515. Found: 300.1511.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.7 mL/min), t_R = 40.8 min (*S*), t_R = 45.72 min (*R*).

(*S*)-1,3-diphenyl-3-*p*-tolylpropan-1-one (2.4a)



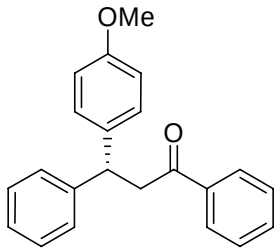
This compound (a pale yellow solid) was prepared in 94% yield from (*E*)-chalcone, diethyl 4-methylphenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ +22.7 (94:6 er, c 1.2, $CHCl_3$)

The spectral data was identical to the data for the *R* enantiomer of this compound.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.7 mL/min), t_R = 38.84 min (*S*), t_R = 42.78 min (*R*).

(*R*)-3-(4-methoxy)-1,3-diphenylpropan-1-one (2.4b)



This compound (a yellow solid) was prepared in 66% yield from (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 10:1.

$[\alpha]^{25}_{589}$ -37.5 (9:91 er, c 2.2, $CHCl_3$)

m.p. 68-71 ^oC

IR (KBr): 1675, 1514, 702 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, J = 7.2 Hz, 2H), 7.54 (t, J = 6.2 Hz, 1H), 7.43 (t, J = 7.2 Hz, 2H), 7.26 (m, 4H), 7.18 (m, 3H), 6.81 (d, J = 8.7 Hz, 2H), 4.79 (t, J = 7.3 Hz, 1H), 3.78 (s, 3H), 3.71 (d, J = 7.3 Hz, 2H)

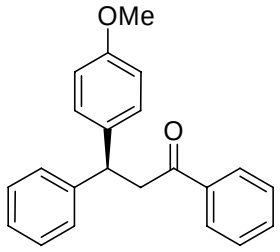
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 158.0, 144.5, 137.0, 136.2, 133.0, 128.7, 128.5, 128.4, 128.0, 127.7, 126.2, 113.9, 55.1, 45.1, 44.8

MS *m/z* (relative intensity): 316 (M^+, 39), 197 (M^+-$PhCOCH_2$, 100), 105 ($PhCO^+$, 10), 77 (Ph^+, 8)

HRMS *m/z* calcd. for $C_{22}H_{20}O_2$ (M^+): 316.1464. Found: 316.1468

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 98.8/1.2, flow rate = 1 mL/min), t_R = 37.96 min (*S*), t_R = 46.02 min (*R*)

(*S*)-3-(4-methoxy)-1,3-diphenylpropan-1-one (2.4b)



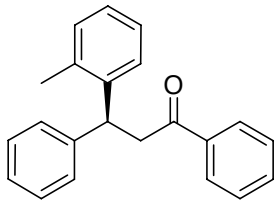
This compound (a yellow solid) was prepared in 88% yield from (*E*)-chalcone, diethyl 4-methoxyphenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 10:1.

$[\alpha]^{25}_{589}$ +57.1 (89:11 er, c 2.8, $CHCl_3$)

The spectral data was identical to the data for the *R* enantiomer of this compound.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 98.8/1.2, flow rate = 1 mL/min), t_R = 34.52 (*S*), t_R = 43.88 (*R*)

(*S*)-1,3-diphenyl-3-*o*-tolylpropan-1-one (2.4c)



This compound (yellow oil) was prepared in 70% yield from (*E*)-chalcone, diethyl 2-methylphenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ +1.5 (95:5 er, c 0.39, $CHCl_3$)

IR (neat): 1686, 1597, 750 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.28-7.19 (m, 4H), 7.17-7.09 (m, 5H), 5.03 (t, J = 7.3 Hz, 1H), 3.80-3.64 (m, 2H), 2.33 (s, 3H)

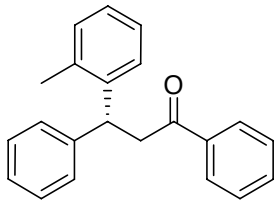
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 143.7, 141.8, 137.0, 136.4, 133.0, 130.7, 128.6, 128.4, 128.0, 127.9, 126.3, 126.2, 126.0, 45.0, 41.8, 19.9

MS *m/z* (relative intensity): 300 (M^+, 32), 282 (100), 196 (21), 181 (M^+-$PhCOCH_2$, 78), 167 (31), 105 ($PhCO^+$, 92), 77 (Ph^+, 24)

HRMS *m/z* calcd. for $C_{22}H_{20}O$ (M^+): 300.1515. Found: 300.1517.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.5/0.5, flow rate = 0.7 mL/min), t_R = 43.67 min (*S*), t_R = 50.02 min (*R*).

(*R*)-1,3-diphenyl-3-*o*-tolylpropan-1-one (2.4c)



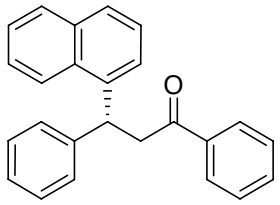
This compound (yellow oil) was prepared in 75% yield from (*E*)-1-phenyl-3-*p*-tolylprop-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ -1.6 (1:99 er, c 2.3, $CHCl_3$)

The spectral data was identical to the data for the *S* enantiomer of this compound.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.7 mL/min), t_R = 49.13 min (*S*), t_R = 52.60 min (*R*).

(*R*)-1,3-diphenyl-3-naphthylpropan-1-one (2.4d)



This compound (a yellow solid) was prepared in 90% yield from (*E*)-3-(naphthalen-4-yl)-1-phenylprop-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 10:1.

$[\alpha]^{25}_{589}$ -2.1 (2:98 er, c 3.8, $CHCl_3$)

m.p. 70-75 ^oC

IR (KBr): 1675, 1597, 688 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (d, J = 9.1 Hz, 1H), 7.93 (d, J = 7.5 Hz, 2H), 7.82 (d, J = 9.4Hz, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.53 (t, J = 7.3 Hz, 1H), 7.44-7.37 (m, 5H), 7.29-7.19 (m, 5H), 7.10 (t, J = 7.2 Hz, 1H), 5.66 (t, J = 7.2 Hz, 1H), 3.86-3.82 (m, 2H)

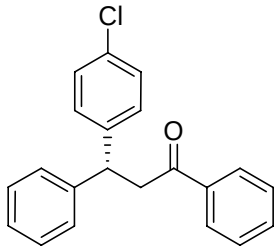
^{13}C NMR (75 MHz, $CDCl_3$): δ 197.9, 143.9, 139.7, 137.0, 134.2, 133.1, 131.6, 128.8, 128.6, 128.5, 128.1, 128.0, 127.3, 126.4, 126.2, 125.6, 125.3, 124.4, 123.8, 45.1, 41.4

MS *m/z* (relative intensity): 336 (M^+, 100), 217 (M^+-$PhCOCH_2$, 98), 215 (35), 105 ($PhCO^+$, 31), 77 (Ph^+, 13)

HRMS *m/z* calcd. for $C_{19}H_{20}O$ (M^+): 336.1515. Found: 336.1505

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 98.7/1.3, flow rate = 1 mL/min), t_R = 46.42 min (*S*), 51.48 min (*R*).

(*R*)-3-(4-chlorophenyl)-1,3-diphenylpropan-1-one (2.4e)



This compound (a pale yellow solid) was prepared in 74% yield from (*E*)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 10:1.

$[\alpha]^{25}_{589}$ -8.2 (9:91 er, c 1.4, $CHCl_3$)

m.p. 83-85 ^{o}C

IR (KBr): 1674, 1595, 1014, 748 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (d, J = 7.4 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.20 (m, 9H), 4.79 (t, J = 6.9 Hz, 1H), 3.69 (d, J = 6.9 Hz, 2H)

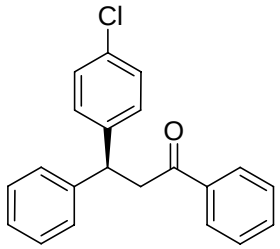
^{13}C NMR (75 MHz, $CDCl_3$): δ 197.6, 143.7, 142.6, 136.8, 133.2, 129.2, 128.6, 128.0, 127.7, 126.6, 45.2, 44.5

MS *m/z* (relative intensity): 320 (M^+, 74), 201 (M^+-$PhCOCH_2$, 71), 165 (31), 105 ($PhCO^+$, 100), 77 (Ph^+, 18)

HRMS *m/z* calcd. for $C_{21}H_{17}{}^{35}ClO$ (M^+): 320.0969. Found: 320.0969.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.7 mL/min), t_R = 52.84 min (*S*), t_R = 66.77 min (*R*)

(*S*)-3-(4-chlorophenyl)-1,3-diphenylpropan-1-one (2.4e)



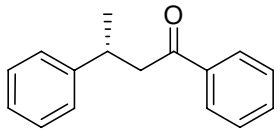
This compound (a pale yellow solid) was prepared in 67% yield from (*E*)-chalcone, diethyl 4-chlorophenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 10:1.

$[\alpha]^{25}_{589}$ +7.9 (91:9 er, c 2.3, $CHCl_3$)

The spectral data was identical to the data for the *R* enantiomer of this compound.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.7 mL/min), t_R = 43.43 min (*S*), t_R = 54.82 min (*R*)

(*R*)-1,3-diphenylbutan-1-one (2.4f)



This compound (a yellow oil) was prepared in 66% yield from (*E*)-1-phenylbut-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ -55.0 (7:93 er, c 0.82, $CHCl_3$)

IR (neat): 2963, 1685, 1001, 755 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.91 (d, J = 7.7 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.3-7.26 (m, 4H), 7.20-7.16 (m, 1H), 3.52-3.43 (m, 1H), 3.28 (dd, J = 16.5 Hz, 5.7 Hz, 1H), 3.16 (dd, J = 16.5 Hz, 8.3 Hz, 1H), 1.32 (d, J = 6.9 Hz)

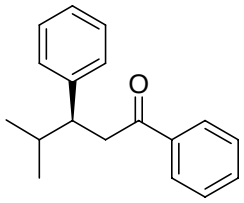
^{13}C NMR (75 MHz, $CDCl_3$): δ 199, 146.5, 137.1, 132.9, 128.5, 128.49, 128.0, 126.8, 126.2, 47.0, 35.5, 21.8

MS *m/z* (relative intensity): 224 (M^+, 40), 209 (M^+-CH_3, 38), 105 ($PhCO^+$, 55), 86 (65), 84 (100), 77 (Ph^+, 20), 51 (34)

HRMS *m/z* calcd. for $C_{16}H_{16}O$ (M^+): 224.1202. Found: 224.1197

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.6/0.4, flow rate = 1 mL/min), t_R = 23.06 min (*S*), t_R = 24.86 min (*R*)

(*R*)-4-methyl-1,3-diphenylpentan-1-one (2.4g)



This compound (a yellow oil) was prepared in 72% yield from (*E*)-4-methyl-1-phenylpent-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ -72.5 (11:89 er, c 0.79, $CHCl_3$)

IR (neat): 2959, 1685, 1597, 701 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, J = 7.1 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 7.21 (d, J = 7.1 Hz, 2H), 7.16-7.10 (m, 3H), 3.33 (d, J = 6.9 Hz, 2H), 3.14 (q, J = 7.1 Hz, 1H), 1.98-1.86 (m, 1H), 0.962 (d, J = 6.7 Hz, 3H), 0.769 (d, J = 6.7 Hz, 3H)

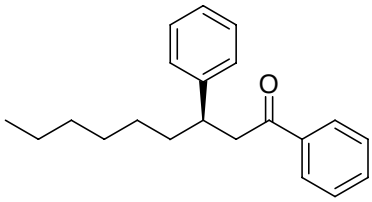
^{13}C NMR (75 MHz, $CDCl_3$): δ 199.2, 143.5, 137.2, 132.7, 128.4, 128.3, 128.0, 127.9, 126.1, 47.8, 42.5, 33.2, 20.9, 20.3

MS *m/z* (relative intensity): 252 (M^+, 4), 209 (M^+-C_3H_7, 32), 132 (M^+-$PhCOCH_2$, 100), 105 ($PhCO^+$, 100), 77 (Ph^+, 27)

HRMS *m/z* calcd. for $C_{18}H_{20}O$ (M^+): 252.1515. Found: 252.1513

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.6/0.4, flow rate = 1 mL/min), t_R = 21.26 min (*S*), t_R = 24.41 (*R*)

(*R*)-1,3-diphenylnonan-1-one (2.4h)



This compound (a pale yellow solid) was prepared in 54% yield from (*E*)-1-phenylnon-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ +28.8 (9:91 er, c 1.13, $CHCl_3$)

m.p. 59-62 ^{o}C

IR (KBr): 2917, 1683, 1594, 699 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88 (d, J = 7.9 Hz, 2H), 7.51 (t, J = 7.3 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.29-7.13 (m, 5H), 3.35-3.27 (m, 1H), 3.24-3.21 (m, 2H), 1.70-1.62 (m, 2H), 1.72 (s, 8H), 0.81 (t, J = 6.6 Hz, 3H)

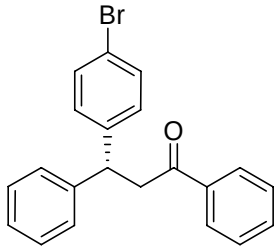
^{13}C NMR (75 MHz, $CDCl_3$): δ 199.2, 145.0, 137.2, 132.8, 128.5, 128.4, 128.0, 127.5, 126.2, 45.9, 41.2, 36.3, 31.7, 29.2, 27.4, 22.6, 14.0

MS *m/z* (relative intensity): 294 (M^+, 18), 209 (M^+-C_6H_{13}, 100), 174 (M^+-$PhCOCH_2$, 100), 105 ($PhCO^+$, 52), 104.1 (23), 77 (Ph^+, 19)

HRMS *m/z* calcd. for $C_{21}H_{26}O$ (M^+): 294.1985. Found: 294.1975.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.6/0.4, flow rate = 1 mL/min), t_R = 15.02 min (*S*), t_R = 18.18 min (*R*).

(*R*)-3-(4-bromophenyl)-1,3-diphenylpropan-1-one (2.4i)



This compound was prepared in 66% yield from (*E*)-3-(4-bromophenyl)-1-phenylprop-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 10:1. After two recrystallizations in hexane, the er was >99:1.

$[\alpha]^{25}_{589}$ -6.3 (>1:99 er, c 0.28, $CHCl_3$)

m.p. 117-118 ^{o}C

IR (KBr): 1677, 1593, 689 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (d, J = 7.9 Hz, 2H), 7.54 (t, J= 7.0 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.26-7.17 (m, 5H), 7.12 (d, J = 8.3 Hz, 2H), 4.77 (t, J = 7.3 Hz, 1H), 3.69 (d, J = 7.3 Hz, 2H)

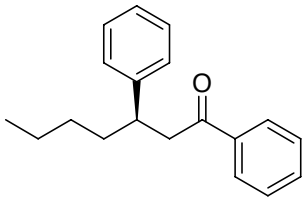
^{13}C NMR (75 Hz, $CDCl_3$): δ 197.6, 143.6, 143.1, 136.8, 133.2, 131.6, 129.6, 128.64, 128.61, 128.0, 127.7, 126.6, 120.2, 45.3, 44.4

MS *m/z* (relative intensity): 364 (M^+, 43), 247 (40), 245 (M^+-$PhCOCH_2$, 42), 165 (32), 105 ($PhCO^+$), 77 (Ph^+)

HRMS *m/z* calcd. for $C_{21}H_{17}{}^{79}BrO$ (M^+): 364.04631. Found: 364.0459.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.8 mL/min), t_R = 73.98 min (*S*), t_R = 92.51 min (*R*)

(*R*)-1,3-diphenyl-heptan-1-one (2.4j)



This compound (a yellow oil) was prepared in 58% yield from (*E*)-1-phenylhept-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 24:1.

$[\alpha]^{25}_{589}$ +86.0 (9:91 er, c 4.0, $CHCl_3$)

IR (neat): 2857, 1685, 1597, 700 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.88 (d, J = 7.8 Hz, 2H), 7.51 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.29-7.16 (m, 5H), 3.32-3.21 (m, 3H), 1.75-1.64 (m, 2H), 1.27-1.10 (m, 4H), 0.80 (t, J = 6.9 Hz, 3H)

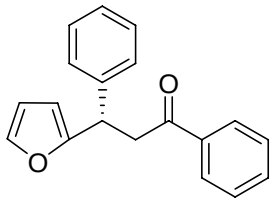
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 145.0, 137.1, 132.8, 128.5, 128.3, 128.0, 127.5, 126.2, 45.9, 41.2, 36.0, 29.6, 22.6, 13.9

MS *m/z* (relative intensity): 266 (M^+, 9), 209 (M^+-C_4H_9, 100), 146 (M^+-$PhCOCH_2$, 98), 117 (18), 105 ($PhCO^+$, 75), 92 (25), 86 (60), 84 (95), 77 (Ph^+, 26), 51 (32)

HRMS *m/z* calcd. for $C_{19}H_{22}O$ (M^+): 266.1672. Found: 266.1668.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.6/0.4, flow rate = 0.8 min/mL), t_R = 20.69 min (*S*), t_R = 26.15 min (*R*)

(*R*)-3-(furan-2-yl)-1,3-diphenylpropan-1-one (2.4k)



This compound was prepared in 28% yield from (*E*)-3-(fran-2-yl)-1-phenylprop-2-en-1-one, diethyl phenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 15:1.

$[\alpha]^{25}_{589}$ -2.6 (98:2 er, c 0.40, $CHCl_3$)

IR (KBr): 1676, 1081, 747 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, J = 7.1 Hz, 2H), 7.54 (t, J = 6.2 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.30-7.20 (m, 6H), 6.26-6.25 (m, 1H), 6.025 (d, J = 3.2 Hz, 1H), 4.83 (t, J = 7.2 Hz, 1H), 3.81 (dd, J = 17.0 Hz, 7.3 Hz, 1H), 3.54 (dd, J = 17.1, 7.1 Hz, 1H)

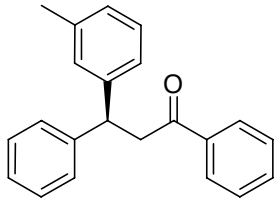
^{13}C NMR (75 MHz, $CDCl_3$): δ 197.4, 156.6, 141.9, 141.4, 136.8, 133.0, 128.5, 128.0, 127.7, 126.7, 110.1, 105.7, 43.5, 40.2

MS *m/z* (relative intensity): 276 (M^+, 71), 171 (-PhCO, 17), 157 (-$PhCOCH_2$, 100), 128 (19), 105 ($PhCO^+$, 44), 77 (Ph^+, 19)

HRMS calcd. for $C_{19}H_{16}O_2$ (M^+): 276.1150. Found: 276.1154

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.7 mL/min), t_R = 31.8 min (*R*), t_R = 76.2 min (*S*)

(*S*)-1,3-diphenyl-3-*m*-tolylpropan-1-one (2.4l)



This compound (a pale yellow solid) was prepared in 73% yield from (*E*)-chalcone, diethyl 3-methylphenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 20:1.

$[\alpha]^{25}_{589}$ +32.3 (99.5:0.5 er, c 0.95, $CHCl_3$)

m.p. 60-62 ^oC

IR (KBr): 1679, 1596, 706 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 7.94 (d, J = 7.9 Hz, 2H), 7.54 (t, J = 7.1 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.27 (d, J = 4.32 Hz, 4H), 7.19-7.14 (m, 2H), 7.08 (d, J = 6.8, 2H), 6.99 (d, J = 7.3 Hz, 1H), 4.80 (t, J = 7.3, 1H), 3.73 (d, J = 7.3 Hz, 2H), 2.29 (s, 3H)

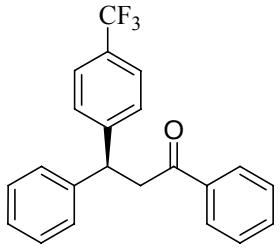
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.0, 144.2, 144.0, 138.0, 137.0, 132.9, 128.6, 128.5, 128.4, 128.3, 128.0, 127.7, 127.1, 126.2, 124.6, 45.8, 44.7, 21.4

MS *m/z* (relative intensity): 300 (M^+, 100), 181 (M^+-$PhCOCH_2$, 77), 165 (24), 105 ($PhCO^+$, 67), 77 (Ph^+, 16)

HRMS *m/z* calcd. for $C_{22}H_{20}O$ (M^+): 300.1515. Found: 300.1509.

The enantiomeric purity was determined by HPLC: (ChiralCel OD, hexane/*i*-PrOH = 99.5/0.5, flow rate = 0.7 mL/min), t_R = 42.53 min (*S*), t_R = 62.49 min (*R*).

(*S*)-1,3-diphenyl-3-(4-trifloromethylphenyl)-propan-1-one (2.4m)



This compound (a pale yellow solid) was prepared in 21% yield from (*E*)-chalcone, diethyl 4-trifluoromethylphenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:dichloromethane 1:3.

$[\alpha]^{25}_{589}$ +8.8 (91:9 er, c 0.5, $CHCl_3$)

m.p. 132-135 ^{o}C

IR (KBr): 1650, 1010, 736 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, J = 7.9 Hz, 2H), 7.58-7.35 (m, 7H), 7.31-7.19 (m, 5H), 4.88 (t, J = 7.2 Hz, 1H), 3.82-3.62 (m, 2H)

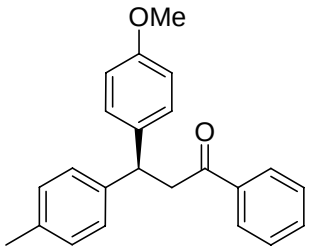
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 148.8, 143.9, 137.5, 134.0, 129.4, 129.3, 128.9, 128.7, 128.4, 127.4, 126.2, 126.1, 46.3, 45.0, 30.4, 1.7

MS *m/z* (relative intensity): 354 (M^+, 52), 235 (-$PhCOCH_2$, 31), 105 ($PhCO^+$, 100), 77 (Ph^+, 21)

HRMS calcd for $C_{22}H_{17}F_3O$ (M^+): 354.1231. Found: 354.1231.

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99.2/0.8, flow rate = 0.7 mL/min), t_R = 43.38 min (*S*), t_R = 57.11 min (*R*)

(S)-3-(4-methoxyphenyl)-1-phenyl-3-p-tolylpropan-1-one (2.5)



This compound (a yellow solid) was prepared in 83% yield from (*E*)-1-phenyl-3-*p*-tolylprop-2-en-1-one, diethyl 4-methoxyphenylboronate and (*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthol using general procedure B and purified by flash chromatography using hexane:ether 6.5:1.

$[\alpha]^{25}_{589}$ -26.7 (89:11 er, c 1.95, $CHCl_3$)

m.p. 83-84 ^{o}C

IR (KBr): 1629, 1114, 1005 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (d, J = 7.5 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.13 (t, J = 8.1 Hz, 3H), 7.05 (d, J = 8.0, 2H), 6.78 (d, J = 8.6, 2H), 4.71 (t, J = 7.3 Hz, 1H), 3.73 (s, 3H), 3.46 (d, J = 7.3 Hz, 2H), 2.26 (s, 3H)

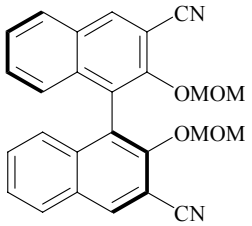
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.2, 157.9, 141.5, 137.1, 136.8, 135.7, 133.0, 129.2, 128.7, 128.5, 128.0, 127.5, 113.9, 55.2, 45.0, 44.7, 20.9

MS *m/z* (relative intensity): 330.3 (M^+, 42), 211.2 (-$PhCOCH_2$, 100)

HRMS calcd. for $C_{23}H_{22}O_2$ (M^+):330.1620 Found: 330.1628

The enantiomeric purity was determined by HPLC analysis: (ChiralCel OD, hexane/*i*-PrOH = 99/1, flow rate = 1 mL/min), t_R = 25.92 min (*S*), t_R = 30.27 min (*R*)

(*S*)-3,3'-dicyano-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (2.2i)



3,3'-Diiodo-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (1 eq, 1.005 g, 1.60 mmol), copper cyanide (4 eq, 0.433 g, 4.80 mmol) and DMF (50 mL) were added to a 100 mL flame-dried flask under an $Ar_{(g)}$ atmosphere. The reaction mixture was heated to 80 ^{o}C and stirred overnight. The reaction was allowed to cool to room temperature, diluted with diethyl ether, then quenched with $NH_4Cl_{(aq)}$ at pH 8 then washed with $NH_4Cl_{(aq)}$ at pH 8 (3 x 50 mL), H_2O (3 x 50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (1/1 Et_2O/hexanes). Yield = 291 mg, 43%.

$[\alpha]^{25}_{589}$ +10.8 (c 0.50, $CHCl_3$)

IR (neat): 1475, 1201, 1031 cm^{-1}

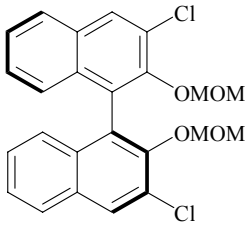
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (s, 2H), 7.95 (d, J = 8.1 Hz, 2H), 7.53 (t, J = 7.4 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 4.92 (d, J = 6.3 Hz, 2H), 4.75 (d, J = 6.4 Hz, 2H), 2.84 (s, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 152.6, 136.9, 135.3, 129.9, 129.6, 128.6, 126.8, 126.1, 125.6, 116.7, 107.6, 99.8, 56.9

MS *m/z* (relative intensity): 424 (M^+, 28), 348 (100), 327 (17), 318 (28)

HRMS *m/z* calcd. for $C_{26}H_{20}N_2O_4$: 424.1423. Found: 424.1428.

(*S*)-3,3'-dichloro-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (2.2j)



2,2'-Bis(methoxymethoxy)-1,1'-binaphthyl (1 eq, 4.2336g, 11.3 mmol) was added to 194 mL of diethyl ether (17 mL/mmol) in a flame-dried flask under $Ar_{(g)}$ atmosphere. *n*-BuLi (24.0 mL of a 1.41 M solution in hexanes, 33.9 mmol, 3eq) was then added to the solution. After the reaction mixture was stirred for three hours the reaction was cooed down to 0°C, then THF (124 mL, 11 mL/mmol) and hexachloroethane (33.9 mmol, 8.0252 g, 3eq) were added to the reaction. It was left to warm up to room temperature overnight. Reaction was quenched with $NH_4Cl_{(aq)}$. The organic layer was isolated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over $Na_2SO_{4(s)}$ and concentrated *in vacuo*. The residue was purified by column chromatography (10:1 hexanes:ether). Yield = 4.04 g, 81%

$[\alpha]^{25}_{589}$ -29.5 (c 3.8, $CHCl_3$)

m.p. 69-70 °C

IR (KBr): 1236, 1156, 818 cm^{-1}

^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (s, 2H), 7.80 (d, J = 8.2 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.28 (t, J = 7.6 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 4.85 (q, J = 5.6 Hz, 4H), 2.59 (s, 6H)

^{13}C NMR (75 MHz, $CDCl_3$): 149.3, 132.6, 130.9, 129.4, 127.6, 127.5, 126.9, 126.7, 126.4, 126.1, 98.9, 56.2

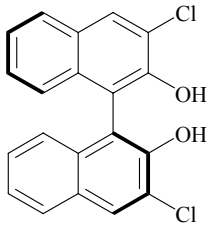
MS *m/z* (relative intensity): 442 (M^+, 27), 366 (100), 303 (27), 268 (20), 84 (18).

HRMS *m/z* calcd. for $C_{24}H_{20}Cl_2O_4$: 442.0740. Found: 442.0756

General Procedure for 3,3'-disubstituted-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl deprotection

The protected disubstituted BINOL was placed in a flask with a 1:1 (v/v) mixture of MeOH (37.5 mL/g):THF and Amberlyst-15 (mass BINOL/mass Amberlyst-15 = 1). The mixture was stirred at reflux overnight, then cooled to room temperature and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography.

(*S*)-3,3'-dichloro-2,2'-dihydroxy-1,1'-binaphthyl (2.2g)



$[\alpha]^{25}_{589}$ -1.1 (c 3.9, THF)

m.p. 176-178 ^{o}C

IR (KBr): 1584, 1146, 814 cm^{-1}

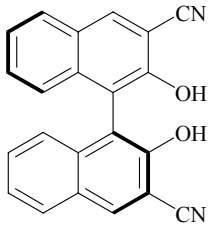
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (s, 2H), 7.80 (d, J = 8.1 Hz, 2H), 7.38 (t, J = 7.2 Hz, 2H), 7.28 (t, J = 7.1 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H), 5.56 (s, 2H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 147.3, 132.2, 129.1, 129.0, 127.4, 127.3, 124.8, 124.5, 122.1, 114.8

MS *m/z* (relative intensity): 354 (M^+, 100), 319 (M^+-Cl, 5), 226 (15), 113 (10).

HRMS *m/z* calcd. for $C_{20}H_{12}Cl_2O_2$: 354.0214. Found: 354.0211

(*S*)-3,3'-dicyano-2,2'-dihydroxy-1,1'-binaphthyl (2.2h)



$[\alpha]^{25}_{589}$ -0.80 (c 2.6, THF)

m.p. >252 ^{o}C

IR (KBr): 2234, 1504, 892 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.41 (s, 2H), 7.95 (d, J = 9.3 Hz, 2H), 7.48 (m, 4H), 7.09 (d, J = 9.2 Hz, 2H), 5.50 (s, 2H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 151.5, 137.7, 134.9, 131.0, 129.3, 128.3, 126.0, 124.1, 111.9, 102.6, 1.01

MS *m/z* (relative intensity): 336 (M^+, 100), 319 (M^+-OH, 7), 279 (8).

HRMS *m/z* calcd. for $C_{22}H_{12}N_2O_2$: 336.0899. Found: 336.0902.

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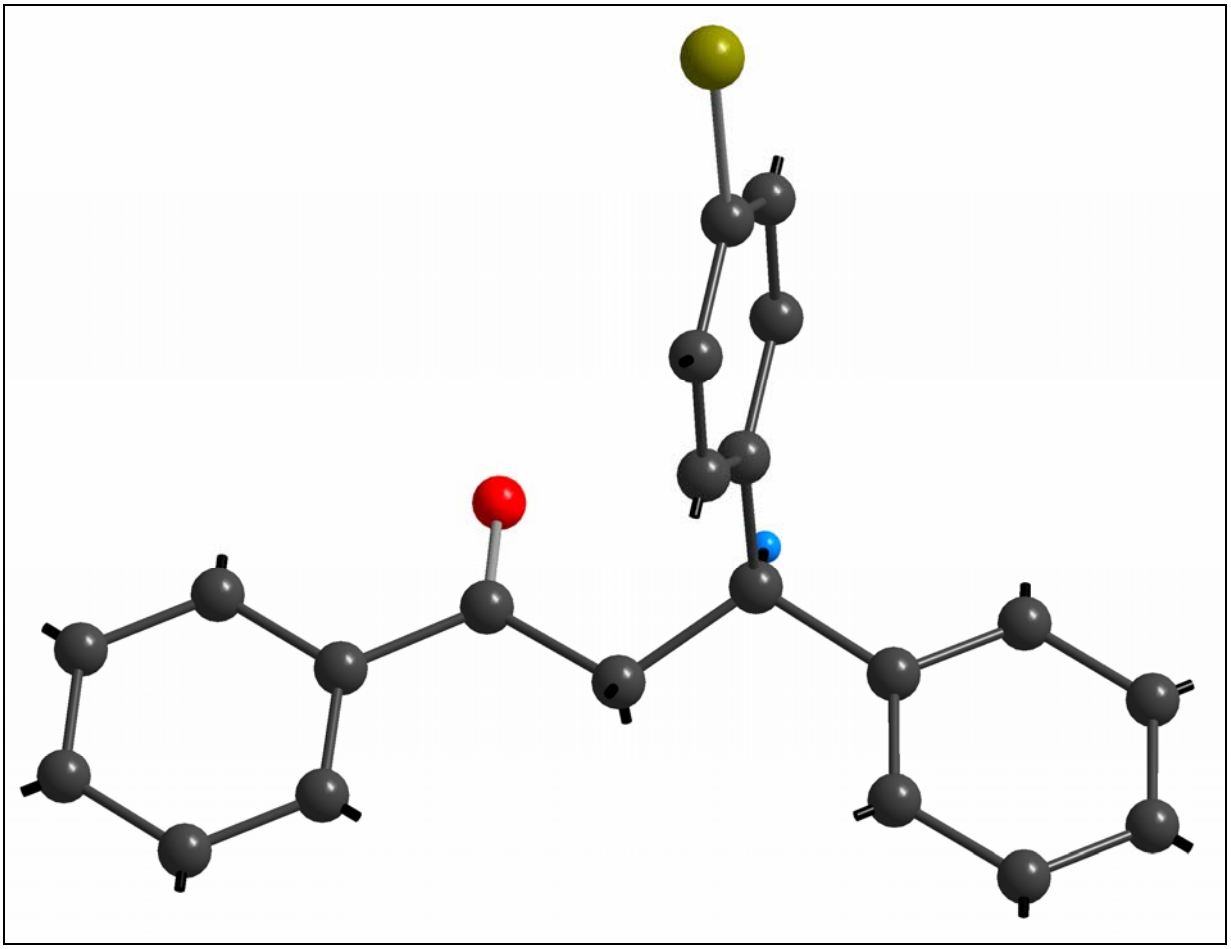
Appendix A: X-ray Crystallography data for (*R*)-3-(4-bromophenyl)-1,3-diphenylpropan-1-one (**2.4i**)



Crystal data and structure refinement for $C_{21}H_{17}BrO$

Empirical formula	$C_{21}H_{17}BrO$
Formula weight	365.26 g/mol
Temperature	200(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Unit cell dimensions	a = 5.7256(18) Å, b = 16.786(5) Å , c = 17.572(6) Å
Volume	1688.8(9) $Å^3$
Z, Calculated density	4, 1.437 g/cm^3
Absorption coefficient	2.436 mm^{-1}
F(000)	744
Crystal size	0.49 x 0.38 x 0.10 mm
Theta range for data collection	3.36 to 28.00 °
Limiting indices	-7<=h<=7, -22<=k<=22, -23<=l<=23
Reflections collected / unique	21751 / 4069 [R(int) = 0.0566]
Completeness to theta = 28.00	99.8 %
Absorption correction	Empirical
Max. and min. transmission	0.7927 and 0.3815
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4069 / 0 / 208
Goodness-of-fit on F^2	1.058
Final R indices [I>2σ(I)]	R1 = 0.0328, wR2 = 0.0758
R indices (all data)	R1 = 0.0428, wR2 = 0.0803
Absolute structure parameter	0.023(8)
Largest diff. peak and hole	0.245 and -0.424 $e.Å^3$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for $C_{21}H_{17}BrO$

	x	y	z	U(eq)
Br(1)	-912(1)	-8387(1)	-342(1)	76(1)
O(1)	3693(3)	-9785(1)	-3682(1)	49(1)
C(1)	1774(4)	-9842(1)	-3973(1)	33(1)
C(2)	62(4)	-10477(1)	-3727(1)	37(1)
C(3)	612(4)	-10829(1)	-2942(1)	32(1)
C(4)	231(3)	-10224(1)	-2311(1)	31(1)
C(5)	1950(4)	-10097(1)	-1763(1)	37(1)
C(6)	1619(4)	-9559(1)	-1174(1)	45(1)
C(7)	-442(4)	-9146(1)	-1135(1)	43(1)
C(8)	-2192(4)	-9260(1)	-1660(1)	43(1)
C(9)	-1853(4)	-9798(1)	-2246(1)	38(1)
C(10)	-740(4)	-11593(1)	-2783(1)	34(1)
C(11)	-2867(4)	-11762(1)	-3114(1)	41(1)
C(12)	-4030(5)	-12474(1)	-2950(1)	48(1)
C(13)	-3076(5)	-13014(1)	-2455(1)	46(1)
C(14)	-962(5)	-12850(1)	-2119(1)	45(1)
C(15)	202(4)	-12144(1)	-2278(1)	40(1)
C(16)	1059(4)	-9295(1)	-4601(1)	31(1)
C(17)	2580(4)	-8676(1)	-4804(1)	36(1)
C(18)	1994(4)	-8167(1)	-5391(1)	41(1)
C(19)	-65(4)	-8264(1)	-5785(1)	41(1)
C(20)	-1587(4)	-8877(1)	-5593(1)	40(1)
C(21)	-1027(4)	-9384(1)	-4999(1)	36(1)
H(2A)	67	-10911	-4108	44
H(2B)	-1528	-10245	-3717	44
H(3A)	2309	-10970	-2939	39
H(5A)	3376	-10385	-1794	44
H(6A)	2802	-9478	-802	54
H(8A)	-3616	-8972	-1621	52
H(9A)	-3058	-9880	-2610	45
H(11A)	-3547	-11392	-3458	50
H(12A)	-5493	-12583	-3183	58
H(13A)	-3869	-13498	-2344	56
H(14A)	-291	-13223	-1777	54
H(15A)	1656	-12036	-2039	48
H(17A)	4011	-8607	-4539	43
H(18A)	3021	-7745	-5524	49
H(19A)	-446	-7912	-6189	50
H(20A)	-3002	-8947	-5867	48
H(21A)	-2079	-9798	-4861	44

Table 3. Bond lengths [Å] and angles [°] for $C_{21}H_{17}BrO$

Br(1)-C(7)	1.908(2)
O(1)-C(1)	1.216(3)
C(1)-C(16)	1.492(3)
C(1)-C(2)	1.512(3)
C(2)-C(3)	1.534(3)
C(3)-C(4)	1.519(3)
C(3)-C(10)	1.524(3)
C(4)-C(5)	1.393(3)
C(4)-C(9)	1.395(3)
C(5)-C(6)	1.388(3)
C(6)-C(7)	1.370(4)
C(7)-C(8)	1.376(3)
C(8)-C(9)	1.384(3)
C(10)-C(11)	1.380(3)
C(10)-C(15)	1.389(3)
C(11)-C(12)	1.398(3)
C(12)-C(13)	1.371(3)
C(13)-C(14)	1.374(4)
C(14)-C(15)	1.389(3)
C(16)-C(21)	1.392(3)
C(16)-C(17)	1.402(3)
C(17)-C(18)	1.380(3)
C(18)-C(19)	1.377(3)
C(19)-C(20)	1.390(3)
C(20)-C(21)	1.384(3)
O(1)-C(1)-C(16)	120.79(19)
O(1)-C(1)-C(2)	121.32(19)
C(16)-C(1)-C(2)	117.87(17)
C(1)-C(2)-C(3)	113.33(17)
C(4)-C(3)-C(10)	110.86(16)
C(4)-C(3)-C(2)	111.66(16)
C(10)-C(3)-C(2)	112.65(16)
C(5)-C(4)-C(9)	118.0(2)
C(5)-C(4)-C(3)	120.30(18)
C(9)-C(4)-C(3)	121.63(18)
C(6)-C(5)-C(4)	121.2(2)
C(7)-C(6)-C(5)	118.9(2)
C(6)-C(7)-C(8)	121.6(2)
C(6)-C(7)-Br(1)	119.71(17)
C(8)-C(7)-Br(1)	118.69(18)
C(7)-C(8)-C(9)	119.2(2)
C(8)-C(9)-C(4)	121.0(2)
C(11)-C(10)-C(15)	118.4(2)
C(11)-C(10)-C(3)	122.94(18)
C(15)-C(10)-C(3)	118.68(18)
C(10)-C(11)-C(12)	120.6(2)
C(13)-C(12)-C(11)	120.5(3)
C(12)-C(13)-C(14)	119.4(2)
C(13)-C(14)-C(15)	120.5(2)

C(14)-C(15)-C(10)	120.7(2)
C(21)-C(16)-C(17)	119.02(18)
C(21)-C(16)-C(1)	122.71(18)
C(17)-C(16)-C(1)	118.25(18)
C(18)-C(17)-C(16)	119.8(2)
C(19)-C(18)-C(17)	120.7(2)
C(18)-C(19)-C(20)	120.17(19)
C(21)-C(20)-C(19)	119.6(2)
C(20)-C(21)-C(16)	120.7(2)